American Journal of Diseases of Children

VOLUME 44 NOVEMBER, 1932 NUMBER 5

LEUKOCYTIC RESPONSE TO MEASLES

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The precise nature of the leukocytic reactions during measles still remains a subject concerning which there are surprising differences of opinion. Although it is generally held that a leukocytosis is present during the incubation period, followed as a rule by a leukopenia during the acute febrile stage,[1] there is a lack of agreement regarding the changes in the differential count. It was early pointed out by several investigators [2] that the fall in the blood count was due chiefly to a diminution in the number of lymphocytes. Diametrically opposed to this finding, however, have been the reports of a lymphocytosis occurring simultaneously with the rash.[3] Moreover, it has been maintained [4] that variations in the number of polymorphonuclear cells principally account for the leukocytosis or the leukopenia observed in the different phases

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1. (*a*) Sobotka, J.: Zur Kenntnis des Vaccineprocesses, Ztschr. f. Heilk. **14**:349, 1893. (*b*) Renaud, A.: La leucocytose dans la rougeole et le rôle clinique de son étude, Thèse de Lausanne, Paris, 1900. (*c*) Uspenski, I. E.: Morfologicheskiya izmïeneniya krovi pri kori, Moscow, 1905. (*d*) Felsenthal, S.: Hämatologische Mittheilungen, Arch. f. Kinderh. **15**:78, 1893. (*e*) Türk, W.: Klinische Untersuchungen über das Verhalten des Blutes bei acuten Infectionskrankheiten, Vienna, Wilhelm Braumüller, 1898, p. 301. (*f*) Reckzeh, P.: Das Verhalten des Blutes bei Masern und Scharlach im Kindesalter, Ztschr. f. klin. Med. **45**:107 and 201, 1902. (*g*) Erben, F.: Klinische Blutuntersuchungen bei Masern, Scharlach, und Varizellen, Ztschr. f. Heilk. **5**:274, 1904. (*h*) Tileston, W.: The Blood in Measles, J. Infect. Dis. **1**:551 (Nov.) 1904. (*i*) Hecker, R.: Cytologische und klinische Beobachtungen während der Maserninkubation, Ztschr. f. Kinderh. **2**:77, 1911. (*j*) Lucas, W. P.: The Value of the Blood Picture in the Early Diagnosis of Measles, Especially in Relation to the Question of Isolation, Am. J. Dis. Child. **7**:149 (Feb.) 1914. (*k*) Rille, J. H.: Ueber morphologische Veränderungen des Blutes bei Syphilis und einigen Dermatosen, Arch. f. Dermat. u. Syph. **24**:1028, 1892. (*l*) Klein, S.: Die diagnostische Verwerthung der Leukocytose, in von Volkmann, R.: Sammlung klinischer Vorträge, Leipzig, Breitroff u. Härtel, 1893, no. 87. (*m*) Platenga: La leucocytose de la rougeole et de la rubéole, Arch. de méd. d. enf. **6**:129 (March) 1903. (*n*) Lagriffoul: La formule leucocytaire de la rougeole et de la rubéole, Arch. de méd. expér. et d'anat. path. **18**:818 (Nov.) 1906.

2. Footnote 1 *d-j*.

3. Footnote 1 *k-n*.

4. Plantenga (footnote 1 *m*). Renaud (footnote 1 *b*).

of the disease. More recent workers,[5] on the other hand, have laid great stress on the lack of uniformity in the blood picture of measles. The confusion arising from the conflicting reports is reflected in the inadequate and contradictory statements found in textbooks on the subject.

The present investigation was undertaken with a view to clarifying this situation. To this end, it was considered essential, first, to study a large number of cases, particularly ones that could be observed daily during incubation and throughout the febrile and convalescent stages. Furthermore, it was apparent that an evaluation of the blood picture in terms of absolute numbers of the different cellular elements would avoid some of the pitfalls encountered by earlier workers. Finally, it seemed likely that the use of the supravital technic would yield more definitive knowledge of the hematologic features of measles than would the previously applied methods of staining.

CASE MATERIAL AND PROCEDURE

The results presented are based on a study of forty-six patients with measles admitted to the hospital of the Rockefeller Institute for Medical Research during the winter and spring of 1930. The importance of making observations on cases early in the incubation period was fully appreciated, and accordingly as large a number as possible of susceptible children known to have been exposed to measles was admitted for observation. The disease developed in twenty of these children at the expected time, and the results of investigations on them constitute the basis for most of the conclusions in this report. The majority of cases in this group were in normal children who had been at home in contact with infected brothers or sisters. Eight were exposed while inmates of a hospital ward. Four of the eight were ill with active infections other than measles and afforded interesting information on the modifications of the blood picture produced by complications. In addition to the early cases, twelve patients were admitted during the period of invasion, two or three days before the outbreak of the eruption. The remaining fourteen were not seen until after the appearance of the rash. Although most of the patients were infants and young children, a few older children and two adults were included in the group of patients studied (table 1).

TABLE 1.—*Age Distribution of Cases*

Counts Begun	9-12 Mos.	1-2 Yrs.	2-3 Yrs.	3-4 Yrs.	4-5 Yrs.	5-6 Yrs.	6-7 Yrs.	7-8 Yrs.	11-12 Yrs.	Adult	Total
Incubation period.....	4	4	4	3	4	..	1	..	..	..	20
Preeruptive period.....	1	3	2	2	1	2	..	..	..	1	12
Eruptive period.....	1	2	3	3	..	1	1	1	1	1	14
Total.....	6	9	9	8	5	3	2	1	1	2	46

5. (*a*) Usbeck, G.: Untersuchungen über das Masernblutbild, Ztschr. f. Kinderh. **36**:182, 1923. (*b*) von Winterfeld, H. K., and Hahne, E.: Ueber die differentialdiagnostische Verwendbarkeit des leukocytären Blutbildes bei Masern und Scharlach, Klin. Wchnschr. **2**:1977 (Oct. 22) 1923. (*c*) Mironescu, T., and Farkas, E.: Erfahrungen bei einer Masernepidemie, Wien. klin. Wchnschr. **39**: 1307 (Nov. 4) 1926. (*d*) Olechnowiez, S.: Recherches sur les globules blancs dans la rougeole, Rev. franç. de pédiat. **5**:209 (April) 1929.

Blood counts were made daily, with certain exceptions, throughout the period of observation in the hospital. So far as it was possible, the counts were made at approximately the same time each morning. The children were examined every day, and careful records were made for the purpose of correlating the hematologic changes with the clinical features of the disease. The number of white cell counts and differentials in positive cases reached a total of 623, of which 433 were performed on the children admitted during the period of incubation.

The usual technic was applied for the estimation of the total number of leukocytes. The blood was diluted in standardized pipets and mixed for three minutes in a mechanical shaking machine. The number of cells in the four corner squares of a standard hemocytometer was counted in making the determination.

The differential counts were made by means of the supravital method. The technic employed did not differ essentially from that described by Sabin.[6] The dyes used were neutral red (National Aniline and Chemical Company) and Janus green (diazine green, National Aniline and Chemical Company). They were kept as saturated solutions in neutral absolute alcohol. A freshly prepared mixture of 2 drops of the stock solution of Janus green and 15 drops of the neutral red solution added to 3 cc. of neutral absolute alcohol was used for flooding the slides. An excellent description of the leukocytes as they appear when stained supravitally with these dyes has been given by Sabin.

Most of the supravital counts in this study were made in a warm box at 37 C. Toward the end of the work this was found to be unnecessary. Indeed, Casey and Rosahn[7] have shown that, although supravital preparations degenerate within an hour or two at 37 C., they keep well for four hours at room temperature and can be preserved intact for twenty-four hours in the icebox. In accordance with the accepted method for supravital differentials, 100 cells were counted for each determination. In making the examinations with the use of a mechanical stage, care was exercised to avoid the peripheral portions of the smear where the preparation is very thick, as well as the center of the smear where the weight of the cover slip exerts the greatest pressure on the cells. Absolute values were calculated from the differential percentages and are given to two significant figures except where the values were less than 100 per cubic millimeter, in which case but one figure is given.

It should be emphasized that the use of Janus green is essential in studying the mononuclear elements of the blood, since it reveals important cytologic characteristics that are not made evident by neutral red alone. It is distinctly helpful, for example, in the differentiation of some types of monocytes. In this connection, it should be borne in mind also that human monocytes differ from the monocytes of some of the laboratory animals in that the presence of a clearly defined rosette of neutral red granules grouped about the centrosphere is usually lacking. More frequently these granules are widely scattered without pattern in the cytoplasm. Occasionally the form of a rather large rosette is suggested by the absence of neutral red bodies toward the periphery of the cell. Cells presenting this appearance are sometimes erroneously considered to be "modified" or "stimulated" monocytes.

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6. Sabin, F. R.: Studies of Living Human Blood-Cells, Bull. Johns Hopkins Hosp. **34**:277 (Sept.) 1923.

7. Casey, A. E., and Rosahn, P. D.: Delayed Differential Counting of the White Blood Cells by a Modified Supravital Technique, Proc. Soc. Exper. Biol. & Med. **28**:658 (March) 1931.

ANALYSIS OF DATA

It has been shown that comparative differential counts carefully made by means of the fixed smear and the supravital methods do not give identical results. Usually the number of polymorphonuclear neutrophils is lower and the lymphocyte count is higher in the fixed than in the supravital preparations, the discrepancy at times being 10 per cent or more.[8] This difference has been attributed chiefly to the destruction of variable numbers of polymorphonuclear cells which appear as unidentifiable smudges in the fixed smears. Indeed, in some pathologic conditions the friability of the polymorphonuclear leukocytes may be so increased as to render counts on pulled smears entirely misleading.[9] The uneven distribution of the cells in the dry preparations, with the tendency for the polymorphonuclear leukocytes to accumulate toward the periphery and to adhere in great numbers to one or the other cover slip, has also been found to alter the constancy of the results obtained by the use of the fixed technic. Still another source of error in counts made on fixed preparations has been shown to lie in the frequent uncertainty in the differentiation of some monocytes from lymphocytes.

The hitherto accepted figures for the different cellular elements of normal blood were thus secured through the use of a method subject to numerous errors. For this reason it has been necessary to make a new table of normal leukocyte values which conforms to the findings obtained by means of the supravital technic. Table 2 represents the results of an attempt to estimate the limits of normal and the average numbers of the different cellular elements in the blood during infancy and childhood, and is based on modifications of the findings, with the fixed smear method, of Karnizki,[10] Carstanjen,[11] Schloss [12] and Perlin.[13] The figures

8. (*a*) Sabin, F. R.; Cunningham, R. S.; Doan, C. A., and Kindwall, J. A.: The Normal Rhythm of the White Blood Cells, Bull. Johns Hopkins Hosp. **37**:14 (July) 1925. (*b*) Rogers, P. M.: A Study of the Blood Monocytes in Children with Tuberculosis, New England J. Med. **198**:740 (May 24) 1928. (*c*) Smith, C. H.: Differential White Count in Infancy: Comparison by Supravital and Fixed Smear Methods, Am. J. Dis. Child. **40**:505 (Sept.) 1930.

9. Lewis, P. A., and Shope, R. E.: The Blood in Hog Cholera, J. Exper. Med. **50**:719 (Dec.) 1929.

10. Karnizki, A. O.: Ueber das Blut gesunder Kinder, Arch. f. Kinderh. **36**:42, 1903.

11. Carstanjen, M.: Wie verhalten sich die procentischen Verhältnisse der verschiedenen Formen der weissen Blutkörperchen beim Menschen unter normalen Umständen? Jahrb. f. Kinderh. **52**:333 (Sept.) 1900.

12. Schloss, O. M.: The Normal Percentages of the Different Varieties of Leukocytes in Infants and Children, Arch. Int. Med. **6**:638 (Dec.) 1910.

13. Perlin, A.: Beitrag zur Kenntnis der physiologischen Grenzen des Hämoglobingehaltes und der Zahl der Blutkörperchen im Kindesalter, Jahrb. f. Kinderh. **58**:549, 1903.

TABLE 2.—*Normal Leukocyte Values Expressed in Absolute Numbers per Cubic Millimeter*

Age	Total White Blood Cells		Polymorphonuclear Neutrophils		Eosinophils		Basophils		Lymphocytes		Monocytes	
	Limits of Normal	Average Normal	Limits of Normal	Average Normal	Limits of Normal	Average Normal	Limits of Normal	Average Normal	Limits of Normal	Average Normal	Limits of Normal	Average Normal
6-12 mos.	8,000-15,000	11,500	2,500-8,000	4,500	80-600	250	0-150	50	3,100-8,300	5,800	500-1,500	900
1- 2 yrs.	7,000-13,000	10,500	2,700-7,000	4,800	70-600	250	0-130	50	3,000-6,600	4,400	500-1,500	900
2- 3 yrs.	7,000-13,000	9,400	3,000-7,000	4,700	70-600	250	0-130	50	2,300-5,600	3,700	500-1,500	700
3- 4 yrs.	7,000-13,000	8,900	3,000-8,000	4,700	70-600	250	0-130	40	2,300-5,500	3,200	400-1,500	700
4- 5 yrs.	7,000-13,000	8,900	3,000-8,000	4,900	70-600	250	0-130	40	2,000-4,800	2,900	400-1,500	800
5- 6 yrs.	7,000-13,000	8,900	3,000-8,000	5,100	70-600	250	0-130	40	1,500-4,800	2,700	400-1,500	800
6- 7 yrs.	5,000-12,000	8,600	2,500-8,000	5,100	50-600	200	0-120	40	1,300-4,500	2,500	300-1,400	800
7- 8 yrs.	5,000-12,000	8,600	2,500-8,000	5,100	50-500	200	0-120	40	1,100-4,500	2,400	300-1,400	800
8- 9 yrs.	5,000-12,000	7,900	2,500-8,000	4,800	50-500	200	0-120	40	1,100-4,500	2,200	300-1,400	700
9-10 yrs.	5,000-12,000	7,900	2,500-8,000	4,800	50-500	200	0-120	40	1,000-4,500	2,200	300-1,400	600
10-11 yrs.	5,000-11,000	7,600	2,500-7,500	4,700	50-500	200	0-110	40	1,000-4,000	2,000	300-1,300	600
11-12 yrs.	5,000-11,000	7,600	2,500-7,500	4,700	50-500	200	0-110	40	1,000-4,000	2,000	300-1,300	600
Adult	5,000-10,000	7,500	3,000-7,000	4,800	50-400	200	0-100	40	900-3,500	1,800	300-1,200	600

chosen from the literature are those agreeing most closely with the results of supravital examinations of the blood of the children observed by us after recovery from measles was fully established. On ten additional normal children daily supravital counts for a period of from two to three weeks were made, and the results were also employed in the determination of the normal standards. The values in the table are expressed in absolute numbers per cubic millimeter of blood.

From table 2 it is seen that the lymphocytes are at their highest level in the peripheral blood during infancy, after which their values drop progressively until the adult figure is reached. The fact that the lymphocyte count, as distinct from that of the other cell types, varies with the age of the subject, must, of course, be borne in mind in interpreting the results. On the other hand, contrary to the prevailing view, the averages for the polymorphonuclear neutrophils are fairly constant during the greater part of infancy and childhood. It is apparent, furthermore, that the normal ranges of monocytes, basophils and eosinophils do not change very much during this period. Because of the closely similar values it is permissible for the purpose of composite analysis to group together, as has been done in this study, the leukocyte counts of children ranging from 9 months to 6 years of age.

The analysis of the data in this paper proceeds on the basis of the foregoing facts. In view of the wide numerical variations in the leukocytic blood elements of healthy persons, a representation, solely by means of average curves, of the changes accompanying disease is manifestly inadequate. The results are therefore recorded (figs. 2, 3 and 10) in such a manner as to indicate the distribution of values of the individual blood counts in addition to the curves of the averages of these counts.[14] In this way, important features, such as maximum and minimum figures and the degree of clumping or dispersion of the plotted values on any given day, are clearly shown.

The charts in figures 1, 2, 3 and 10 represent the results of observations, begun during the incubation period of measles, on a group of sixteen otherwise normal children. In the construction of the graphs, the blood counts were plotted with reference to the first day of fever as a fixed point rather than to the more variable time of appearance of the rash. The blood counts made on two of the children after they had developed secondary bronchopneumonia and acute otitis media,[15] respec-

14. The curves obtained by plotting the averages were smoothed in the usual manner according to the formula $\frac{a + 2b + c}{4}$

15. Pathologic changes in the appearance of the ear-drums without suppuration are as characteristic of uncomplicated measles as are pharyngitis and bronchitis. In this group of cases, when cultures from the middle ear revealed the presence of pathogenic micro-organisms, however, the otitis media was looked on as a complicating factor.

tively, are not included in the charts. Thus, the graphic analyses are limited to uncomplicated cases. In the discussion of the results, the findings in this group of sixteen children are considered first and then are supplemented by data from other cases observed at the same time.

RESULTS

To facilitate a description of the leukocytic changes found in the blood of patients with measles, the disease is divided into three periods, namely, the incubation, febrile and convalescent stages. Variations in the total leukocyte count together with those of each of the different cell types as they occur in these three phases of the malady are presented.

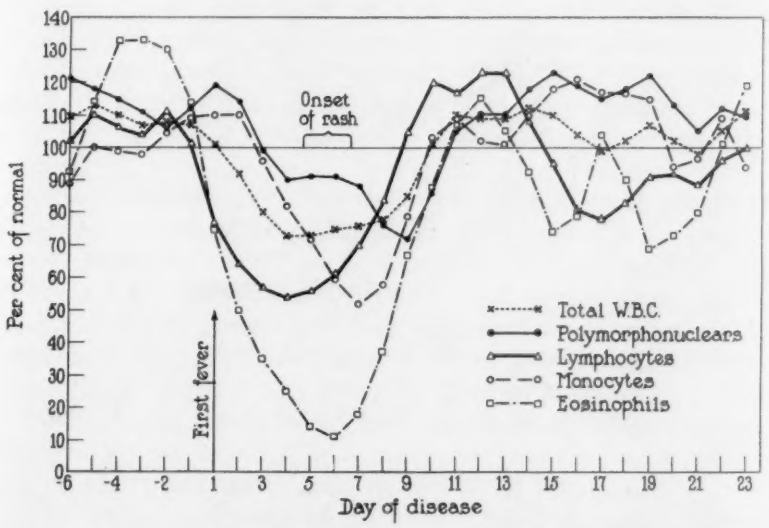

Fig. 1.—Composite analysis of the leukocytic reactions during the course of uncomplicated measles. The curves represent the averages of the blood counts in sixteen cases and are charted to show the comparative percentage deviations from the calculated normal. *First fever* indicates the onset of the period of invasion.

Incubation Period.—Total White Blood Cells: There is an apparent tendency to the development of leukocytosis during the incubation period of measles (fig. 1). This is, however, by no means a constant phenomenon. Only five of twelve cases manifested a clearcut leukocytosis of from 14,000 to 19,000 during this period (figs. 4, 5 and 6), the time of onset of the high blood count varying from one to six days before the inception of fever. Moreover, in no case did the leukocytosis persist longer than three days, and in three of the cases the increase was present on but a single day. Of the cases in which leukocytosis did not develop, all but three (cases 6 and 9, figs. 6 and 8, and case 11,

table 3) showed a tendency to develop high normal counts at some time during this period. These reactions account for the fact that the composite curve for the white blood cells during the incubation stage is somewhat above the normal average level (fig. 1). Nevertheless, the

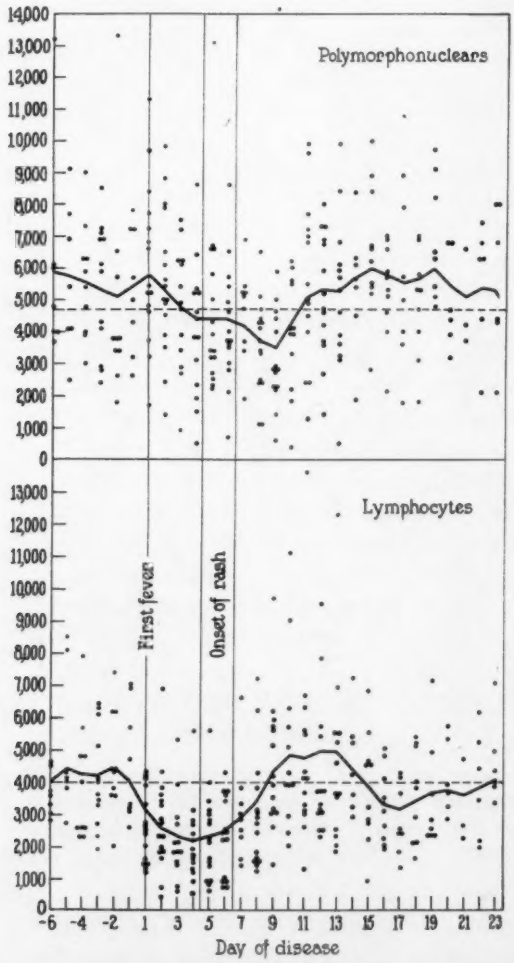

Fig. 2.—Reactions of polymorphonuclear leukocytes and lymphocytes during the course of uncomplicated measles. The curves represent the averages of the blood counts in sixteen cases, the individual counts being plotted as separate points. The calculated normal level is shown in each instance by a broken line. *First fever* indicates the onset of the period of invasion.

idea of Renaud,[1b] who believed it possible to diagnose measles during this stage on the basis of the leukocytosis that begins immediately after the infection is contracted, is not substantiated by this investigation.

The inconstancy of the leukocytosis, its ephemeral nature and the variability in the time of its appearance largely nullify the diagnostic value of this test.

The influence of complications during the incubation period on the blood picture was studied in four cases. A leukocytosis such as was found in the presence of severe pyogenic infections (fig. 9 and case 17, table 3) is not surprising and cannot be attributed to measles. The possibility that measles might have accentuated the degree of the leukocytosis in these cases could not be satisfactorily demonstrated. In one case of active pulmonary tuberculosis (case 20, table 3) the white blood cell count remained entirely normal during this period.

Polymorphonuclear Neutrophils: An analysis of the numerical variations in the polymorphonuclear neutrophils is exceedingly difficult because of the wide daily fluctuations that frequently occur. The variations on successive days may be greater than 100 per cent even though the counts are made at the same hour. In some cases, however (e. g., case 20, table 3), the level of neutrophils may remain remarkably constant.

From an examination of the chart in figure 2, in which the different cell counts are plotted as individual dots, it appears that the points are evenly distributed within the normal limits of from 2,500 to 8,000. However, a few abnormally high values scattered on different days are present and were observed in four cases that showed transient polymorphonucleosis. For this reason the average curve (figs. 1 and 2) during this period is a little above the standard normal line. A study of the neutrophil curves in the individual cases nevertheless points to the fact that the polymorphonuclear leukocytes remain for the most part within normal limits during the prefebrile stage.

The polymorphonucleosis of complicating pyogenic infections (case 17, table 3) completely obscured the polymorphonuclear reaction to measles during the incubation stage. The case of pulmonary tuberculosis (case 20, table 3), on the other hand, showed normal polymorphonuclear leukocyte counts during the incubation period.

Polymorphonuclear Band Forms: Although it is not feasible in supravital preparations to make counts according to the method of Arneth,[16] the most important classes[17] of neutrophilic leukocytes are, nevertheless, capable of being accurately differentiated. In this study the segmented forms, the band forms and the metamyelocytes are separately classified.

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16. Arneth, J.: Die qualitative Blutlehre, Leipzig, Dr. Werner Klinkhardt, 1920. Flesch, H., and Schossberger, A.: Ueber die Veränderung des neutrophilen Blutbildes im Inkubationsstadium von Masern, Jahrb. f. Kinderh. **64**:724 (Nov.) 1906.

17. Schilling-Torgau, V.: Kritik der Arnethschen Lehre von der Verschiebung des leukozytären Blutbildes und Wertung ihrer klinischen Anwendbarkeit, Folia haemat. **12**:130, 1911.

TABLE 3.—*Blood Counts in Illustrative Cases*

Cases	Date	Total White Blood Cells	Polymorphonuclear Neutrophils: Absolute Number	Total per Cent	Per Cent Band Forms	Per Cent Non-motiles	Eosinophils: Absolute Number	Per Cent	Basophils: Absolute Number	Per Cent	Lymphocytes: Absolute Number	Total per Cent	Per Cent Small	Per Cent Intermediate	Per Cent Large	Monocytes: Absolute Number	Per Cent	Miscellaneous Cells, per Cent	Comment
2: a white girl, aged 2 years, with uncomplicated measles (fig. 4)	4/ 5/30	12,700	6,900	54	..	..	250	2	...	..	4,100	32	28	4	..	1,500	12	..	
	4/ 7/30	11,100	7,100	64	1	..	...	..	...	..	3,300	30	28	2	..	670	6	..	
	4/ 8/30	11,000	5,700	52	1	..	...	..	...	..	4,300	39	31	8	..	990	9	..	
	4/ 9/30	13,700	7,800	57	..	..	140	1	...	..	4,700	34	31	3	..	1,100	8	..	
	4/10/30	14,100	9,700	69	6	6	...	..	...	..	2,400	17	14	3	..	2,000	14	..	Onset of fever
	4/11/30	14,600	9,800	67	3	7	...	..	...	..	2,800	19	13	6	..	1,900	13	1*	
	4/12/30	11,100	7,500	68	2	..	...	..	...	..	2,100	19	17	2	..	1,400	13	..	
	4/14/30	4,600	3,400	73	3	35	...	..	...	..	920	20	18	2	..	320	7	..	Koplik's spots; prodromal rash; coryza
	4/15/30	6,400	5,400	85	4	8	...	..	...	..	900	14	13	..	1	60	1	..	Rash of measles
	4/16/30	8,700	6,900	79	15	8	...	..	...	..	1,600	18	11	6	1	260	3	..	
	4/17/30	5,400	3,700	69	7	..	50	1	...	..	1,500	27	15	8	4	50	1	2*	Temperature normal
	4/18/30	6,200	2,200	35	4	..	60	1	...	..	3,000	49	22	18	9	870	14	1*	
	4/19/30	10,700	3,900	36	4	3	...	..	...	..	5,700	53	17	30	6	960	9	2*	
	4/21/30	10,600	6,900	65	..	8	210	2	320	3	2,300	22	11	6	5	850	8	..	
	4/22/30	13,200	9,900	75	2	7	...	..	...	..	2,500	19	11	3	5	790	6	..	
	4/23/30	9,400	5,700	61	..	8	90	1	90	1	2,900	31	18	11	2	560	6	..	
	4/24/30	13,000	10,000	77	..	24	260	2	...	..	2,200	17	12	4	1	520	4	..	
	4/25/30	11,000	7,000	64	1	..	...	..	...	..	3,100	28	20	6	2	880	8	..	
	4/26/30	12,500	8,900	71	..	..	...	..	...	..	2,400	19	14	3	2	1,300	10	..	
	4/28/30	12,300	9,100	74	..	7	...	..	...	..	2,300	19	16	3	..	860	7	..	
4: a white boy, aged 6 years, with uncomplicated measles (fig. 5)	5/15/30	7,800	3,900	50	..	1	860	11	...	..	2,300	30	30	..	..	550	7	2*	
	5/16/30	12,100	8,500	70	1	1	360	3	...	..	2,700	22	18	4	..	600	5	..	
	5/17/30	8,500	3,400	40	2	1	1,200	14	...	..	3,600	42	38	4	..	340	4	..	
	5/19/30	5,600	3,200	57	3	25	390	7	60	1	1,300	24	21	3	..	620	11	..	Onset of fever
	5/20/30	3,300	2,400	72	1	1	200	6	30	1	360	11	10	1	..	330	10	..	Prodromal rash; sneezing
	5/21/30	5,500	3,900	70	8	39	170	3	...	..	720	13	10	3	..	770	14	..	Koplik's spots; conjunctivitis
	5/22/30	5,000	3,100	61	11	4	...	..	...	..	1,200	24	20	3	1	750	15	..	Rash of measles
	5/23/30	4,300	3,400	80	4	51	...	..	...	..	560	13	12	1	..	300	7	..	
	5/24/30	4,700	3,600	77	29	15	...	..	50	1	710	15	14	1	..	330	7	..	
	5/26/30	5,200	3,300	64	6	5	100	2	...	..	1,400	26	14	7	5	420	8	..	Temperature normal
	5/27/30	6,100	4,000	66	..	12	240	4	...	..	1,400	23	17	5	1	430	7	..	
	5/28/30	7,200	3,900	54	9	15	140	2	...	..	2,000	28	17	8	3	1,200	16	..	
	5/29/30	10,800	7,700	71	13	3	760	7	...	..	1,300	12	10	2	..	970	9	1†	
	5/30/30	8,300	4,600	56	2	34	500	6	80	1	2,500	30	25	5	..	580	7	..	
	5/31/30	7,000	3,900	55	1	..	840	12	...	..	1,800	26	21	5	..	420	6	1†	
	6/ 2/30	7,300	5,500	75	..	46	370	5	...	..	880	12	6	5	1	580	8	..	
	6/ 3/30	8,500	5,300	62	9	2	260	3	260	3	1,900	22	17	5	..	770	9	1†	
	6/ 4/30	7,400	3,600	48	..	..	440	6	150	2	2,500	34	28	4	2	740	10	..	
	6/ 5/30	10,400	5,800	56	..	..	730	7	...	..	2,800	27	20	5	2	1,000	10	..	

7: a white boy, aged 2 years, with measles followed by secondary broncho-pneumonia (fig. 7)	4/19/30	9,400	4,100	44	..	..	280	3	90	1	4,000	43	41	2	..	850	9	..	
	4/21/30	9,100	2,800	31	..	13	270	3	90	1	5,100	56	45	11	..	820	9	..	
	4/22/30	11,300	3,800	34	2	5	680	6	...	..	6,200	55	40	13	2	570	5	..	
	4/23/30	12,900	5,000	39	..	..	260	2	130	1	7,000	54	41	13	..	390	3	1*	
	4/24/30	11,400	7,200	63	..	..	110	1	...	..	3,300	29	26	2	1	800	7	..	Onset of fever
	4/25/30	12,700	8,800	69	..	41	...	..	...	..	2,000	16	14	2	..	1,800	14	1*	Prodromal rash; Koplik's spots
	4/26/30	8,800	2,700	31	2	6	...	..	...	..	5,300	60	50	9	1	790	9	..	Coryza; conjunctivitis
	4/28/30	5,900	2,700	46	2	11	...	..	...	..	2,700	45	41	4	..	530	9	..	Rash of measles
	4/29/30	5,500	3,000	54	5	44	...	..	...	..	2,400	43	36	6	1	170	3	..	
	4/30/30	6,300	4,700	74	11	6	...	..	...	..	1,400	22	17	3	2	250	4	..	
	5/ 1/30	7,900	5,100	64	16	36	...	..	...	..	2,700	34	27	6	1	160	2	..	Onset of pneumonia
	5/ 2/30	9,000	5,500	61	..	..	...	..	...	..	3,200	36	24	8	4	270	3	..	
	5/ 3/30	12,700	8,400	66	3	54	...	..	...	..	3,300	26	21	4	1	760	6	2*	
	5/ 5/30	10,800	5,600	52	..	14	110	1	...	..	4,000	37	31	4	2	1,100	10	..	
	5/ 6/30	14,200	8,700	61	20	3	140	1	...	..	3,800	27	25	1	1	1,600	11	..	
	5/ 7/30	21,500	14,000	65	..	..	...	..	...	..	6,500	30	29	1	..	1,100	5	..	
	5/ 8/30	17,500	12,100	69	18	..	350	2	...	..	4,000	23	18	3	2	700	4	2†	Temperature normal
	5/ 9/30	15,500	10,200	66	3	23	160	1	...	..	4,200	27	24	3	..	780	5	1*	
	5/10/30	10,000	5,400	54	6	14	600	6	...	..	3,200	32	20	9	3	700	7	1†	
	5/12/30	9,100	3,000	33	4	2	180	2	...	..	4,900	54	41	9	4	1,000	11	..	
	5/13/30	9,100	3,100	34	4	3	90	1	180	2	4,900	54	45	9	..	820	9	..	
	5/14/30	11,000	4,700	43	3	17	...	..	110	1	5,200	47	37	9	1	880	8	1*	
	5/15/30	6,600	3,100	47	..	6	70	1	70	1	3,000	46	39	6	1	330	5	..	
	5/16/30	7,000	2,500	36	..	6	140	2	70	1	3,600	51	38	11	2	700	10	..	
	5/17/30	7,000	2,700	38	2	..	...	..	70	1	3,600	52	46	6	..	630	9	..	
	5/19/30	7,800	3,400	43	5	6	80	1	...	..	3,500	45	40	5	..	860	11	..	
	5/20/30	5,300	1,800	34	..	2	50	1	...	..	2,900	55	48	6	1	530	10	..	
	5/21/30	8,900	2,300	26	..	..	90	1	...	..	5,700	64	57	6	1	800	9	..	
	5/22/30	9,000	4,100	45	1	3	90	1	...	..	4,100	45	43	1	1	810	9	..	
	5/23/30	8,800	2,800	32	..	..	90	1	90	1	4,800	55	47	8	..	970	11	..	
	5/24/30	7,800	3,700	48	2	..	160	2	230	3	3,400	43	37	4	2	310	4	..	
	5/26/30	5,800	1,600	28	2	..	120	2	...	..	3,800	65	57	7	1	290	5	..	
8: a white boy, aged 21 mos., with uncomplicated measles (fig. 7)	4/25/30	10,000	6,500	65	11	8	100	1	...	..	2,500	25	23	2	..	900	9	..	
	4/26/30	8,100	4,000	49	8	2	240	3	80	1	2,800	35	31	4	..	730	9	3†	
	4/28/30	13,100	6,300	48	..	..	260	2	130	1	4,800	37	28	9	..	1,300	10	1†; 1*	
	4/29/30	11,300	6,900	61	..	16	230	2	110	1	3,600	32	29	3	..	450	4	..	
	4/30/30	8,600	3,800	44	1	8	170	2	...	..	3,800	44	42	2	..	690	8	1†; 1*	
	5/ 1/30	6,100	2,600	42	1	1	120	2	...	..	2,600	43	39	4	..	790	13	..	
	5/ 2/30	7,800	5,400	69	..	24	80	1	...	..	1,400	18	14	4	..	940	12	..	Onset of fever
	5/ 3/30	6,300	3,500	56	..	3	60	1	...	..	1,900	30	29	1	..	820	13	..	
	5/ 5/30	7,100	5,300	74	2	1	...	..	...	..	1,500	21	19	2	..	360	5	..	Koplik's spots; prodromal rash
	5/ 6/30	5,900	3,900	66	2	..	60	1	...	..	1,400	24	21	3	..	470	8	1*	Rash of measles
	5/ 7/30	6,700	3,700	55	2	53	...	..	...	..	2,500	37	35	2	..	270	4	4*	
	5/ 8/30	4,700	1,900	40	14	14	90	2	...	..	2,500	54	48	..	6	90	2	2*	Temperature normal
	5/ 9/30	3,800	1,100	28	6	1	40	1	...	..	2,400	63	46	15	2	300	8	..	
	5/10/30	5,800	2,700	46	..	11	60	1	60	1	2,600	44	31	11	2	350	6	2*	
	5/12/30	10,200	4,000	39	..	8	100	1	100	1	5,500	54	51	3	..	510	5	..	
	5/13/30	7,800	2,700	34	3	1	230	3	...	..	3,700	48	43	5	..	860	11	1*	
	5/14/30	8,300	3,200	39	2	7	250	3	80	1	3,600	43	37	6	..	1,100	13	1†	
	5/15/30	10,600	6,300	59	..	53	...	..	...	..	3,200	30	21	8	1	950	9	2*	
	5/16/30	11,000	5,200	47	1	10	...	..	...	..	4,600	42	32	9	1	1,200	11	..	
	5/17/30	8,300	4,000	48	..	4	...	..	80	1	3,500	42	40	2	..	750	9	..	

* Degenerating cells.
† Metamyelocytes.

TABLE 3.—*Blood Counts in Illustrative Cases—Continued*

Cases	Date	Total White Blood Cells	Polymorphonuclear Neutrophils				Eosinophils		Basophils		Lymphocytes					Monocytes		Miscellaneous Cells, per Cent	Comment
			Absolute Number	Total per Cent	Per Cent Band Forms	Per Cent Non-motiles	Absolute Number	Per Cent	Absolute Number	Per Cent	Absolute Number	Total per Cent	Per Cent Small	Per Cent Intermediate	Per Cent Large	Absolute Number	Per Cent		
8: (continued)	5/19/30	10,100	4,700	47	19	12	200	2	...	..	3,900	39	28	10	1	1,100	11	1†	
	5/20/30	8,200	4,500	58	4	33	...	..	...	..	2,800	34	25	9	..	490	6	2*	
	5/21/30	8,700	4,700	54	4	..	...	..	90	1	3,200	37	33	1	3	700	8	..	
	5/22/30	7,200	4,200	58	2	..	220	3	70	1	2,200	30	26	4	..	500	7	1*	
	5/23/30	7,500	2,100	28	2	..	230	3	80	1	4,400	58	53	5	..	750	10	..	
	5/24/30	6,600	2,100	32	..	3	200	3	...	..	3,900	59	59	..	..	330	5	1‡	
	5/26/30	7,300	2,600	35	1	..	220	3	70	1	3,500	48	45	2	1	950	13	..	
10: a white boy, aged 9 mos., with uncomplicated measles (fig. 8)	6/ 3/30	9,200	4,000	44	1	19	280	3	...	..	4,600	50	40	10	..	280	3	..	
	6/ 4/30	13,700	4,100	30	..	20	...	..	...	..	8,500	62	56	5	1	1,100	8	..	
	6/ 5/30	13,400	4,000	30	1	..	130	1	...	..	7,900	59	52	5	2	1,200	9	1§	
	6/ 6/30	11,700	2,900	25	4	11	470	4	350	3	6,400	55	42	12	1	1,500	13	..	
	6/ 7/30	8,000	1,800	23	..	5	320	4	...	..	4,400	55	47	6	2	1,400	17	1#	
	6/ 9/30	5,800	1,700	30	8	4	230	4	120	2	2,500	43	25	15	3	1,200	20	1*	Onset of fever
	6/10/30	5,200	1,400	27	9	4	50	1	50	1	2,700	51	38	12	1	990	19	1#	
	6/11/30	4,500	900	20	6	9	...	..	90	2	2,900	65	49	16	..	590	13	..	Coryza
	6/12/30	3,800	530	14	4	9	...	..	...	..	2,700	71	47	24	..	570	15	..	Prodromal rash
	6/13/30	5,000	2,200	44	19	11	...	..	...	..	2,100	42	33	8	1	700	14	..	Rash of measles; Koplik's spots
	6/14/30	5,100	710	14	..	13	...	..	...	..	3,700	72	45	19	8	610	12	2*	
	6/16/30	11,100	2,400	22	12	..	...	..	110	1	7,200	65	5	40	20	1,200	11	1*	6/15/30, temperature normal
	6/17/30	12,400	620	5	2	..	500	4	120	1	9,700	78	40	30	8	1,400	11	1†	
	6/18/30	12,600	380	3	..	..	...	..	...	..	11,100	88	55	30	3	1,100	9	..	
	6/19/30	16,400	1,300	8	1	5	...	..	...	..	13,600	83	51	28	4	1,500	9	..	
	6/20/30	12,500	1,400	11	..	11	130	1	...	..	9,500	76	38	33	5	1,400	11	1#	
	6/21/30	16,000	480	3	2	1	...	..	...	..	12,300	77	43	30	4	3,000	19	1*	
11: a white girl, aged 9 mos., with uncomplicated measles	4/19/30	10,100	6,100	60	17	14	...	..	100	1	3,300	33	30	3	..	610	6	..	
	4/21/30	9,800	6,300	64	9	41	200	2	...	..	2,600	27	21	6	..	690	7	..	
	4/22/30	6,700	4,300	64	5	5	270	4	...	..	1,900	29	19	10	..	200	3	..	
	4/23/30	7,800	3,800	49	2	1	...	..	...	..	3,600	46	41	3	2	390	5	..	
	4/24/30	8,400	4,300	51	4	..	250	3	170	2	3,300	39	35	4	..	420	5	..	
	4/25/30	10,200	6,600	65	18	8	....	..	200	2	2,700	26	22	3	1	710	7	..	Onset of fever; coryza
	4/26/30	8,200	3,900	47	2	..	160	2	80	1	3,600	44	40	4	..	410	5	1*	Koplik's spots
	4/28/30	8,100	4,400	54	6	28	...	..	80	1	3,100	38	36	2	..	490	6	1*	Conjunctivitis; prodromal rash
	4/29/30	9,100	5,000	55	9	12	...	..	90	1	4,000	44	34	8	2	.....	..	..	Rash of measles
	4/30/30	7,200	2,800	39	2	10	...	..	...	..	4,300	60	53	6	1	70	1	..	
	5/ 1/30	7,100	3,400	48	12	20	...	..	70	1	3,300	46	42	4	..	210	3	2*	
	5/ 2/30	8,000	4,300	54	5	6	80	1	...	..	3,000	38	33	4	1	480	6	1#	
	5/ 3/30	9,600	4,600	48	1	11	190	2	...	..	4,200	44	29	12	3	580	6	..	Temperature normal
	5/ 5/30	14,200	6,800	48	1	..	140	1	140	1	4,100	29	22	5	2	2,800	20	1*	

17. a white boy, aged 3 yrs., with measles developing during the course of active pulmonary tuberculosis and acute proteus bacillus otitis media and mastoiditis (fig. 9)	4/19/30	13,700	7,800	57	8	34	140	1	140	1	3,000	22	19	3	..	2,600	19	..	
	4/21/30	20,000	14,200	71	4	19	200	1	200	1	4,000	20	15	4	1	1,400	7	..	Temperature septic
	4/22/30	27,800	21,700	78	9	4	...	..	...	..	2,800	10	10	..	..	3,300	12	..	
	4/23/30	43,200	32,000	74	6	46	430	1	430	1	7,800	18	16	2	..	2,600	6	..	
	4/24/30	22,600	19,400	86	6	61	...	..	450	2	1,100	5	4	..	1	1,600	7	..	Sharp rise in temperature
	4/25/30	20,000	16,000	80	2	64	...	..	400	2	1,800	9	8	1	..	1,800	9	..	Prodromal rash
	4/26/30	20,900	15,500	74	1	70	210	1	210	1	4,000	19	15	2	2	1,000	5	..	Koplik's spots
	4/28/30	15,500	12,900	83	4	..	160	1	...	..	1,400	9	6	2	1	1,100	7	..	
	4/29/30	18,200	16,000	88	3	72	...	..	...	..	1,500	8	8	..	..	550	3	1*	Rash of measles
	4/30/30	18,100	15,000	83	..	71	180	1	...	..	2,400	13	10	3	..	540	3	..	
	5/ 1/30	13,400	11,000	82	40	..	400	3	...	..	1,200	9	9	..	..	670	5	1†	Rash faded
	5/ 2/30	14,400	10,900	76	1	..	140	1	140	1	2,200	15	9	5	1	860	6	1†	
	5/ 3/30	18,900	12,300	65	2	46	...	..	190	1	4,000	21	15	4	2	2,100	11	2*	
	5/ 5/30	17,100	10,800	63	..	3	170	1	170	1	3,800	22	13	6	3	2,200	13	..	
	5/ 6/30	15,300	10,300	67	3	..	...	..	...	..	3,100	20	10	7	3	2,000	13	..	
	5/ 7/30	20,600	12,800	62	2	..	410	2	...	..	4,500	22	19	2	1	2,900	14	..	
20: a negro boy, aged 4 yrs., with measles developing during the course of afebrile active pulmonary tuberculosis	4/19/30	8,700	5,600	64	4	3	170	2	90	1	1,800	21	19	1	1	1,000	12	..	
	4/21/30	7,400	4,200	57	5	14	...	..	...	..	2,000	27	18	8	1	1,200	16	..	
	4/22/30	7,700	4,500	59	3	52	80	1	...	..	2,400	31	25	5	1	690	9	..	
	4/23/30	7,700	5,400	70	10	12	80	1	230	3	1,400	18	12	6	..	620	8	..	Onset of fever
	4/24/30	7,500	5,500	73	1	11	...	..	230	3	1,400	18	14	4	..	380	5	1*	
	4/25/30	6,500	5,500	84	8	28	...	..	70	1	460	7	7	..	..	520	8	..	
	4/26/30	3,500	2,200	63	9	..	40	1	40	1	980	28	24	4	..	250	7	..	4/27/30, Koplik's spots; coryza
	4/28/30	5,500	3,700	68	15	2	...	..	...	..	1,500	28	23	3	2	220	4	..	Prodromal rash; conjunctivitis
	4/29/30	5,200	4,300	83	6	51	...	..	...	..	570	11	11	..	..	310	6	..	Rash of measles
	4/30/30	4,900	3,300	68	7	11	...	..	50	1	1,400	29	22	4	3	.....	..	2*	
	5/ 1/30	4,500	3,000	67	4	23	90	2	50	1	1,000	23	14	3	6	270	6	1†	Temperature normal
	5/ 2/30	4,000	2,300	58	..	..	80	2	...	..	1,400	35	28	7	..	200	5	..	
	5/ 3/30	4,900	3,000	62	..	24	150	3	50	1	1,300	26	17	7	2	290	6	1#; 1*	5/4/30, fever again; acute otitis media
	5/ 5/30	7,400	4,100	55	5	2	220	3	150	2	2,100	29	19	9	1	810	11	..	
	5/ 6/30	5,900	3,400	58	..	..	60	1	...	..	1,700	28	24	1	3	710	12	1#	
	5/ 7/30	8,000	4,200	53	7	37	...	..	80	1	3,000	38	29	7	2	640	8	..	
	5/ 8/30	7,000	4,600	66	1	..	...	..	70	1	1,800	26	23	2	1	490	7	..	
	5/ 9/30	9,600	7,200	75	5	53	...	..	...	..	1,600	17	13	4	..	670	7	1*	
	5/10/30	7,800	4,300	55	..	..	160	2	80	1	2,800	36	33	2	1	470	6	..	
	5/12/30	8,900	6,500	73	14	17	...	..	90	1	1,400	16	13	2	1	890	10	..	
32: a white woman, aged 24 yrs., with uncomplicated measles	4/ 6/30	7,300	6,100	84	16	27	...	..	...	..	660	9	8	1	..	510	7	..	Fever; Koplik's spots; prodromal rash
	4/ 7/30	7,800	5,500	71	27	15	80	1	...	..	1,200	16	11	5	..	780	10	2*	
	4/ 8/30	7,400	6,400	87	54	1	...	..	70	1	670	9	5	3	1	220	3	..	Rash of measles
	4/ 9/30	8,700	7,500	86	40	..	...	..	...	..	960	11	7	4	..	170	2	1*	
	4/10/30	7,800	6,800	87	26	28	80	1	..	..	780	10	7	2	1	160	2	..	
	4/11/30	5,700	3,300	58	13	26	110	2	...	..	2,100	36	24	8	4	170	3	1*	Temperature normal
	4/12/30	4,900	2,500	51	9	1	250	5	...	..	1,600	32	19	9	4	590	12	..	
	4/14/30	6,900	4,700	68	2	3	...	..	...	..	1,300	19	13	6	..	900	13	..	
	4/16/30	10,300	7,100	69	5	12	...	..	100	1	2,100	20	13	2	5	930	9	1†	
	4/17/30	12,000	8,800	73	..	..	...	..	...	..	2,500	21	15	3	3	720	6	..	
	4/18/30	10,900	9,000	83	..	2	...	..	...	..	1,100	10	9	1	..	760	7	..	
	4/19/30	11,600	9,600	83	..	1	...	..	350	3	1,000	9	4	4	1	580	5	..	
	4/21/30	9,500	7,200	76	..	..	100	1	100	1	1,600	17	14	2	1	380	4	1*	
	4/22/30	9,000	6,600	73	..	..	180	2	90	1	1,800	20	16	3	1	270	3	1†	

* Degenerating cells.
† Metamyelocytes.
‡ Unstained clasmatocytes.
§ B myelocytes.
# Unclassified cells.

It is evident that during the incubation period the number of band forms is not significantly increased (fig. 10), and no metamyelocytes were observed.

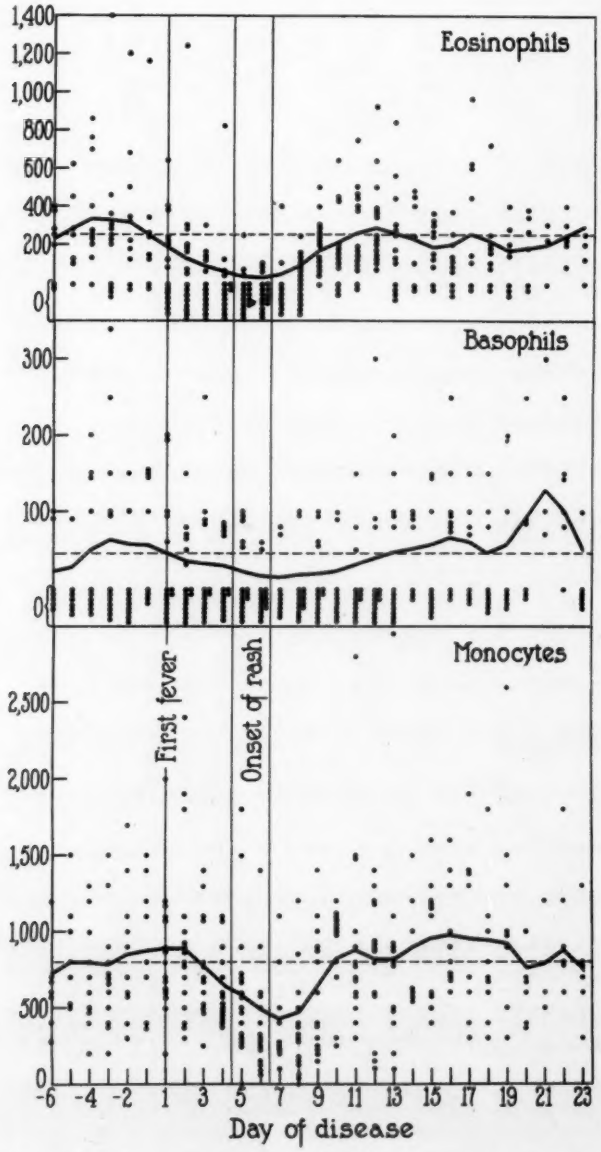

Fig. 3.—Reactions of eosinophils, basophils and monocytes during the course of uncomplicated measles. The curves represent the averages of the blood counts in sixteen cases, the individual counts being plotted as separate points. The calculated normal level is shown in each instance by a broken line. *First fever* indicates the onset of the period of invasion.

Eosinophils: The charted eosinophil counts (fig. 3) reveal a definite deviation from the normal during the incubation period. The curve is seen to rise four days before the onset of the febrile period and to remain well elevated for two days before falling again to the normal level. The fact that an eosinophilia occurs during this stage of the disease is substantiated by an examination of the curve of eosinophils in individual instances. Half of the cases (cases 4, 7 and 10, table 3) showed a distinct rise in the number of eosinophils from two to five days before the beginning of fever. In most instances the increase was above the normal limit of 600 cells per cubic millimeter. In but one case, however, did the count remain elevated on successive days. The cases in which eosinophilia did not develop showed either normal counts (cases 8 and 11, table 3) or different degrees of eosinopenia (case 2, table 3) during the prefebrile stage. Although it is thus seen that the development of an eosinophilia in any given case is uncertain, the time of its first appearance in positive cases seems to bear a more or less constant relationship to the onset of fever.

A point of interest arises in connection with the influence of complications on the eosinophil picture. It is well recognized that infections in general produce a decrease in the number of eosinophils. Complicating infections might, therefore, be expected to interfere with the development of an eosinophilia during the incubation period of measles. Despite this possibility, however, one case showed a striking eosinophilia of 900 cells per cubic millimeter four days before what was considered on other grounds to be the probable beginning of the prodromal period of measles. This reaction occurred in a 4 year old boy (case 18) who was ill with a severe hemolytic streptococcus otitis media. Eosinophilia failed to develop in the other complicated cases, although in case 17 (table 3) there was a rise from a previous level of 80 to 430 cells one day before the inception of fever.

Basophils: Figure 3 shows a considerable number of high basophil counts occurring during the incubation period of measles. The average curve, furthermore, appears to indicate the development of basophilia at this stage. A certain amount of caution must, however, be exercised in interpreting the results of this study of the basophil reactions during measles. To attain an accuracy for the basophil counts comparable to that for the other cellular blood elements, it would be necessary to count at least 500 cells in making each supravital differential analysis. With the technic as it was employed in this work, the finding of 1 or 2 basophils among 100 cells results in a count that may be inordinately high for the blood as a whole. Conversely, the absence of basophils in such a count does not necessarily mean their complete disappearance from the peripheral circulation. The significance of individual counts

in a single case is thus rather doubtful. Nevertheless, the curve of the average of all cases may well give some indication of what changes the basophils undergo during measles. From such an analysis, therefore, it appears that the basophils are perhaps somewhat increased during the incubation period.

The incidence of complications in the group of cases studied is too small to make it profitable to discuss their effect on the basophil count.

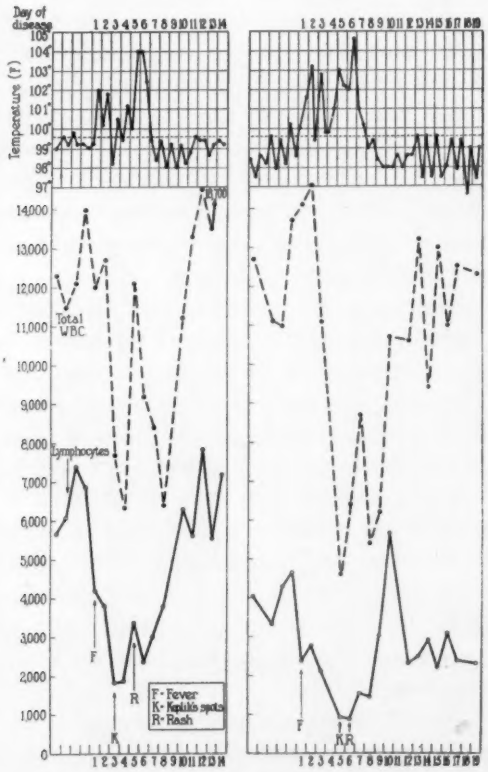

Fig. 4 (cases 1 and 2).—Total white blood cell and lymphocyte counts in two uncomplicated cases first observed during the incubation period of measles. Case 1 (left) was that of a boy, aged 3 years; case 2 (right), that of a girl, aged 2 years (the complete counts in this case are given in table 3). In all the charts, *F* indicates the first fever of the prodromal period; *K*, the appearance of Koplik's spots and *R*, the appearance of the rash. For comparison with normal leukocyte values, see table 2.

Lymphocytes: As in the case of the polymorphonuclear leukocytes, the chart of the lymphocytes (fig. 2) during the first phase of measles shows a fairly even distribution of the plotted values within normal limits. Nevertheless, if one remembers that the upper limit of normal becomes progressively lower during each succeeding year of life

(table 2) one notes that during the period of incubation there are several high values (above 6,000), which represent the development of a lymphocytosis in three cases (cases 1, 7 and 10, figs. 4, 7 and 8). Study of the individual lymphocyte reactions reveals three additional cases (cases 4, 6 and 8, figs. 5, 6 and 7) that showed rising normal values at this time. The remainder, with the exception of one case to which reference is made later, did not deviate from the normal. In the majority of instances, therefore, the lymphocytes varied within normal limits during the incubation period.

Despite the influence of complicating pyogenic infections in three cases, the development of a lymphocytosis during the incubation period in two instances (cases 17 and 18, fig. 9) was not prevented. In one case of active tuberculosis (case 20, table 3) the opposite effect was observed, the lymphocytes failing to rise above low normal figures.

Monocytes: The curve of the monocytes (fig. 3) for the incubation period differs from that of any of the other leukocytes. It begins to rise two days before the beginning of the febrile stage and continues to be elevated for several days. During this entire period, however, the counts fall within normal limits. In the analysis of the response in the individual cases, it is seen that in some instances an increase in the number of monocytes did not appear until the first or second day of prodromal fever (e. g., cases 2 and 7, table 3), and in four cases a rise in the monocyte count was not observed (cases 4 and 11, table 3).

Pyogenic infections did not appear to alter the characteristics of the monocyte curve. Each of the three complicated cases of this group showed decidedly high monocyte counts toward the end of the incubation period (case 17, table 3). Indeed, from a quantitative aspect the change in these cases was more striking than that in the normal group. The high values were 3,300, 2,100 and 1,800, respectively. Nevertheless, in view of the meager knowledge of the effect of pyogenic infections on the monocytes in the absence of measles, this observation must be accepted with some reservation.

It is now well established through the work of Sabin and others [18] that tuberculosis produces profound changes in the monocytic blood picture. In the light of this fact it is of some interest to note the influence of such an infection on the monocyte reaction in measles. The equally interesting possible influence of measles on the blood picture in tuberculosis could not be satisfactorily studied because it was impossible

18. Cunningham, R. S.; Sabin, F. R.; Sugiyama, S., and Kindwall, J. A.: The Rôle of the Monocyte in Tuberculosis, Bull. Johns Hopkins Hosp. **37**:231 (Oct.) 1925. Rogers (footnote 8 *b*). Blackfan, K. D., and Diamond, L. K.: The Monocyte in Active Tuberculosis: Supravital Studies of the Blood, Am. J. Dis. Child. **37**:233 (Feb.) 1929.

to follow the patients for a sufficiently long period. Two cases furnish information regarding the first point. One case of clinically active tuberculosis in a boy of 4 years (case 20, table 3) showed a monocyte response that did not differ from that in the uncomplicated series. In the other case, that of a 3 year old boy who had a severe acute proteus bacillus mastoiditis as well as active tuberculosis (case 17, table 3), the monocyte rise during this period was markedly accentuated.

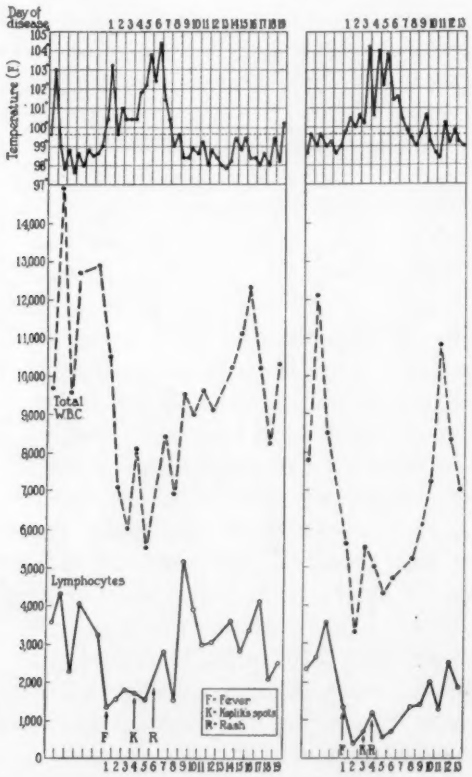

Fig. 5 (cases 3 and 4).—Total white blood cell and lymphocyte counts in two uncomplicated cases first observed during the incubation period of measles. Case 3 (left) was that of a boy, aged 16 months; case 4 (right), that of a boy, aged 6 years (the complete counts in this case are given in table 3).

Fever During the Incubation Period: Some observations on the temperature reactions during the incubation period may be worthy of mention at this point. Since the incubation period of measles is ordinarily characterized by the absence of febrile signs, it was rather surprising that in three of the children unexplained fevers of from 101 to 103 F. developed during this period (cases 3, 5 and 10, figs. 5, 6 and 8). The

children at this time seemed perfectly well, were active and had good appetites. Curiously enough the rise of temperature in each instance occurred six days before the beginning of the period of invasion and lasted for one or two days. In four additional cases slight rises in temperature of from 100 to 100.4 F. were recorded from four to six days before the onset of the prodromal period. These intervals of fever were usually followed by subnormal temperatures on the days immediately preceding the beginning of the prodromal period. The occurrence of such rises in temperature during the incubation period of measles has been noted by Thomas,[19] who referred to them as "ephemera" or "ephemera protracta," and by Heubner,[20] Hecker [21] and others. According to Orel,[21] fever during the incubation period is attributable not to the action of measles virus, but to the action of a bacterial infection contracted at the same time.

Febrile Period.—The leukocytic changes occurring during measles can best be understood if it is realized that the entire febrile period represents one phase of the disease. From this point of view the development of the eruption on the fourth to seventh day of fever appears as merely an incident in the evolution of this period and does not represent the beginning of a new stage. Indeed, the fact that the whole period of fever is ordinarily only from five to eight days long [22] (figs. 4 to 8) points to the possibility that the appearance of the rash marks the end of the infection even though the fever is then at its height.

As will be evident from the results presented in this article, the most striking leukocytic change occurs on the first day of the febrile period. This association of a characteristic alteration of the blood picture with the first rise in temperature is a matter of considerable diagnostic importance, for it is well known that recognition of measles at this stage is frequently impossible.[23] In the group of twenty children

19. Thomas, L.: Beiträge zur Kenntnis der Masern, Arch. d. Heilk. **8**:385, 1867.

20. Heubner, O.: Lehrbuch der Kinderheilkunde, ed. 2, Leipzig, Johann Ambrosius Barth, 1906, vol. 1, p. 279.

21. Orel, H.: Das Verhalten der Körpertemperatur bei Masern zur Zeit der Infektion und während der Inkubation, Ztschr. f. Kinderh. **40**:623 (Feb.) 1926.

22. It appears that the development of events and the duration of the febrile period vary in different epidemics and may have been different in the past. Compare with the temperature charts in Nothnagel, H.: Spezielle Pathologie und Therapie, Vienna, Alfred Hölder, 1896, vol. 4, pt. 2.

23. (*a*) Flindt, N., cited by von Jürgensen, T.: Masern, in Nothnagel, H.: Spezielle Pathologie und Therapie, Vienna, Alfred Hölder, 1896, vol. 4, pt. 2. (*b*) Herrman, C.: Measles: Incubation, Infectivity, Immunity, Early Manifestations, Arch. Pediat. **31**:885 (Dec.) 1914.

observed in this study, Koplik's spots were not present in a single instance on the first day of fever. (The variable time of appearance of this sign is shown in the charts of individual cases, figs. 4 to 9.) Catarrhal symptoms and prodromal rashes on the first day of fever were likewise entirely absent. Nor were any other signs [24] that have been considered to be more or less pathognomonic of measles found to be of value in establishing the diagnosis at this time. In the absence of diag-

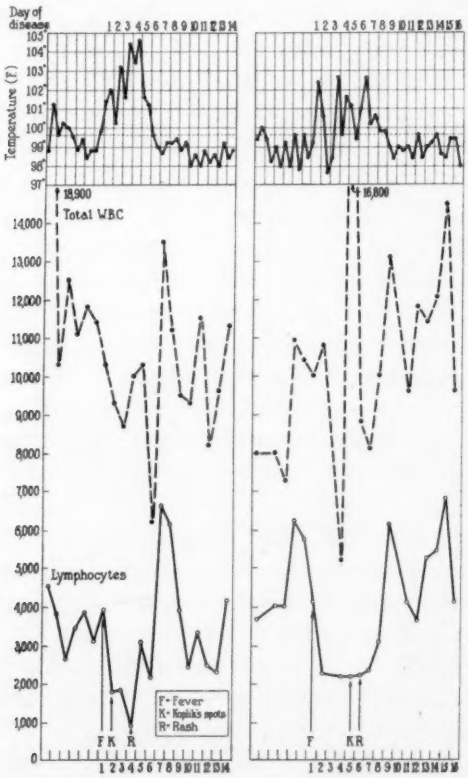

Fig. 6 (cases 5 and 6).—Total white blood cell and lymphocyte counts in two uncomplicated cases first observed during the incubation period of measles. Case 5 (left) was that of a boy, aged 2 years; case 6 (right), that of a boy, aged 17 months (the complete counts in this case are given in table 3).

nostic signs, therefore, increased significance attaches to the reaction manifested by the lymphocytes and to the evolution of the lymphocyte curve as contrasted with that of the other cell types.

24. Herrman (footnote 23*b*); Stimson, P. M.: The Earlier Diagnosis of Measles, J. A. M. A. **90**:660 (March 3) 1928. Petényi, G.: Ein neues Symptom der Masern: Das hämorrhagische Präenanthem, Monatschr. f. Kinderh. **45**:61 (Sept.) 1929.

Total White Blood Cells: From its moderately raised level during the incubation period, the curve of the total white cell count (fig. 1) drops to the normal level on the first day of fever. The average number of leukocytes then falls steadily for three days to reach its low level of 7,300 cells. In the majority of cases, this point is reached on the fourth day of the disease, from twenty-four to forty-eight hours before the appearance of the eruption, following which the curve flattens out and maintains a leukopenic level until the end of the febrile period.

While this was the general trend for the group as a whole, important variations were noted in the individual cases particularly on the first and second days of fever. Five cases showed high, even rising, white blood counts on the first two days of this period (cases 1, 2 and 7, figs. 4 and 7). In four cases, on the other hand, the leukocytes fell sharply to the point of leukopenia at the very beginning of the febrile stage (cases 4, 8, 9 and 10, figs. 5, 7 and 8). The counts in the remaining seven cases conformed to the computed curve (cases 3, 5 and 6, figs. 5 and 6). After the first two days of fever, in all cases a more or less definite leukopenia developed. However, temporary fluctuations in the number of white blood cells, sometimes quite marked, occurred rather frequently even in uncomplicated cases (figs. 4 and 6). Consequently, studies of the white blood count in measles that were based on isolated determinations may be responsible for some of the confusion in the literature on this subject.

The leukopenia of measles is thus seen to be a phenomenon variable in the time of its onset and in the manner of its development. The most marked lowering of the count is generally present on the fourth or fifth day of fever, but in individual instances it may occur anywhere between the second and the eighth days.

The discussion at this point of the effect of complications on the white blood count includes only the cases in which the added infection was present at the beginning of the febrile period. The cases in which the complicating illness appeared at the end of the febrile period are considered in another section. Two children in the group had active pyogenic infections during the entire febrile period of measles. Their charts are of interest for they demonstrate that while the complicating infections might have prevented the development of actual leukopenia, a marked fall in the blood count was nevertheless brought about through the agency of the measles virus (fig. 9). In a third case, one of active tuberculosis (case 20, table 3), the total leukocyte reaction did not differ from that in typical uncomplicated cases.

Polymorphonuclear Neutrophils: An examination of the chart in figure 2 discloses a rather marked spreading out of the plotted values for polymorphonuclear leukocytes on the first day of fever. Fairly

evenly spaced dots representing polymorphonuclear cell counts ranging from 1,700 to 11,300 are seen. However, because there are but three values below 4,000 (cases 4 and 10, table 3), while the majority of points fall above 5,000, the neutrophil curve rises at the onset of the febrile period. On the other hand, the wide spacing of the plotted points as compared with their more confined distribution on the preceding days indicates that the polymorphonuclear reaction on the first day of this period is quite variable. Following the initial tendency during this

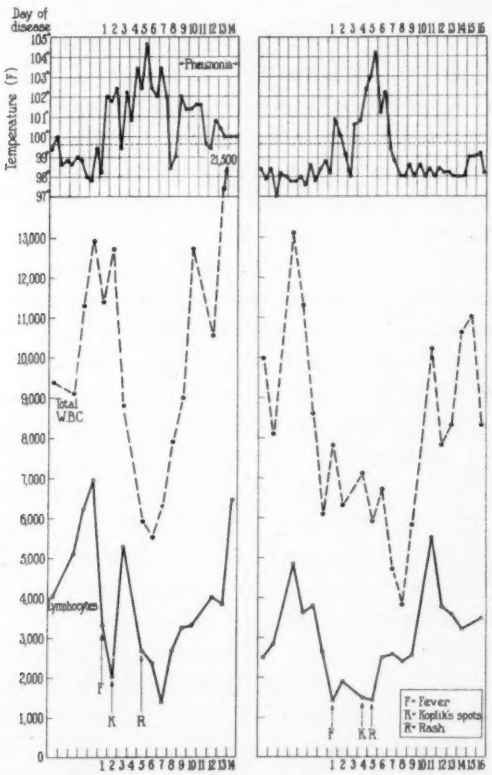

Fig. 7 (cases 7 and 8).—Total white blood cell and lymphocyte counts in two cases first observed during the incubation period of measles. Case 7 (left) was that of a boy, aged 2 years; case 8 (right), that of a boy, aged 21 months (the complete counts in both cases are given in table 3).

phase of the disease for the curve (figs. 1 and 2) to rise, there is a gradual fall until the lowest point is reached on the ninth day. The minimum in the curve coincides with the beginning of convalescence and occurs three or four days after the appearance of the rash.

The polymorphonuclear cell counts in individual cases for the most part followed the trend exhibited by the average curve (cases 2, 7 and 8,

table 3). Rather marked fluctuations were noted, however, particularly about the time of onset of the rash. While sharp increases in the number of neutrophils developed in five cases at this time, neutropenic values below 3,000 were present in four others. Very exceptional reactions were observed in two cases; one (case 4, table 3) showed the lowest polymorphonuclear count on the second day of fever, while in the other (case 10, table 3) neutropenia developed, beginning two days before the febrile onset and continuing throughout the period of observation in the hospital.

In two cases pyogenic infections were responsible for a persistent polymorphonucleosis throughout the febrile period (case 17, table 3). Although the neutrophil curve was thus continually at a high level, its shape in general resembled that of the average curve for the uncomplicated cases. On what seemed to be the first day of the febrile period of measles the polymorphonuclear leukocytes in each case were at a higher point than at any other time during this period. After this, the counts in each case declined steadily, and, again as in the simple cases of measles, the low point was reached on the eighth or ninth day. The neutrophil curve of the patient with the tuberculous infection (case 20, table 3) conformed even more closely to the type of reaction observed in uncomplicated cases.

Polymorphonuclear Band Forms: No important change in the number of young polymorphonuclear leukocytes is noticeable before the fourth day of the febrile period (fig. 10). At this time the curve rises sharply and continues to be elevated during the fifth, sixth and seventh days, that is to say, during the time of appearance of the rash. Following this it rapidly falls again to normal. A pronounced shift to the left in the polymorphonuclear cell group is thus seen to mark the height of the disease.

Among the individual cases the rise in the number of band forms accompanying the rash was observed with considerable regularity. In a few instances, however, increased numbers of band forms were noted earlier in the illness, although usually not before the second or third day of fever. Very young cells of the polymorphonuclear series, such as metamyelocytes, were frequently observed in small numbers at the height of the illness. In rare instances myelocytes appeared in the blood.

Nonmotile Leukocytes: In supravital blood preparations a characteristic type of degenerating polymorphonuclear leukocyte that does not stain with either of the dyes is often seen. This type of cell, which Sabin [6] has designated as the nonmotile leukocyte, is characterized by loss of ameboid motion, by edema and shapelessness of the nucleus and by swelling and high refractility of the granules of the cytoplasm. There is no doubt that the presence of such cells frequently results from

excessive pressure of the cover slip on the polymorphonuclear neutrophils. Because of this pressure, even in the best preparations small areas devoid of all blood cells are regularly produced near the center of the smear, and in the immediate neighborhood of such bare areas all of the polymorphonuclear cells are of the nonmotile type. It has, nevertheless, been maintained that these cells are produced also in the circulating blood and represent the final stage in the life cycle of the

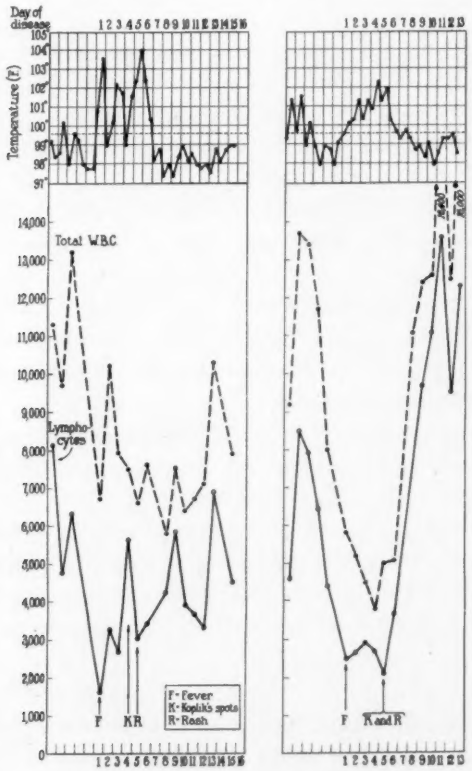

Fig. 8 (cases 9 and 10).—Total white blood cell and lymphocyte counts in two uncomplicated cases first observed during the incubation period of measles. Case 9 (left) was that of a girl, aged 11 months; case 10 (right), that of a boy, aged 9 months (the complete counts in this case are given in table 3).

neutrophil.[8] In support of this contention it has been pointed out that at times normal polymorphonuclear cells and nonmotile leukocytes are seen in the same microscopic field. In view of the latter possibility, an effort was made to determine whether during measles an alteration in the number of nonmotile leukocytes could be ascertained. That these cells might be significantly involved in this disease was, moreover, sug-

gested by the work of Hecker [11] and Lucas,[13] who reported an increase in the number of degenerated neutrophils at the height of the disease. From figure 10 it appears that there is an increase in nonmotile leukocytes at the time of the eruption, and again one week later. The plotted values, however, are too irregularly scattered to permit of any definite conclusions.

Other varieties of degenerative change in the polymorphonuclear leukocytes were not observed in simple measles. When such changes do occur, as in one case of fatal hemolytic streptococcus sepsis following measles, they may be quite striking. In this case, in an infant of 9 months, leukocytes of the "nonmotile" variety were not present. On the other hand, all of the polymorphonuclear cells were definitely abnormal in appearance. Their cytoplasm seemed to be watery, and the cells were in consequence spread out over unusually large areas. Their outlines, moreover, were quite indistinct, and there was little evidence of ameboid activity. Although the character of the nuclei was that of adult cells, the specific neutrophilic granules were, nevertheless, few in number, quite small and poorly defined. Some of the cells in addition contained a few red-staining vacuoles. The fact that nonmotile leukocytes were not found in this case, in which toxic degeneration was so prominent a feature, seems to cast doubt on the validity of the view that the presence of such cells is due in part to the influence of toxic products.

Eosinophils: A sharp drop in the composite curve of the eosinophils (fig. 3) on the first day of fever was brought about by the absence of eosinophils from the blood smears in seven of the cases. The number of such zero counts steadily mounted to a maximum on the fifth and sixth days of the fever. There is thus a progressively increasing tendency for the eosinophils to disappear from the circulating blood during the febrile period of measles. The three high values plotted on the chart (fig. 3) for this period represent the counts of one exceptional case in which eosinophilia persisted until the rash made its appearance. Complicating infections apparently failed to modify the character of the eosinophil response.

Basophils: The basophil curve declines gradually during the febrile period to reach its lowest point on the seventh day (composite curve, fig. 3). That this change is not merely a "relative" phenomenon dependent on the low total white blood counts is evident from figure 3. On each of the sixth, seventh and eighth days, only two counts showed any basophils at all. In individual cases, for reasons already given, the reaction is rather difficult to evaluate. In certain instances, however, the decrease was quite striking (cases 8 and 17, table 3).

Lymphocytes: In marked contrast to the behavior of the polymorphonuclear cells during this stage of the disease, the plotted values for lymphocytes become suddenly clumped on the first day of fever (fig. 2). Moreover, while the neutrophil count continues to rise, the lymphocytes manifest a sharp decrease in numbers concurrent with the onset of the febrile period. The lymphocyte curve then steadily falls until the fourth day of fever, when the lowest point is reached. Not

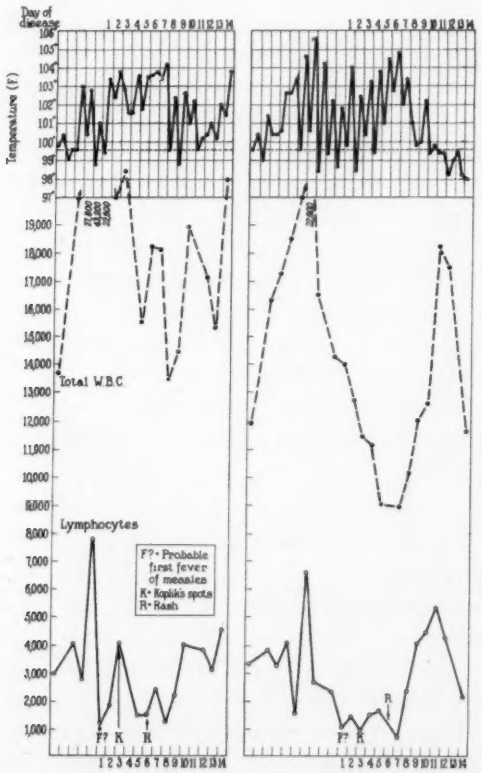

Fig. 9 (cases 17 and 18).—Total white blood cell and lymphocyte counts in two cases of measles in which the reactions were modified by complicating infections already present during the incubation period. Case 17 (left) was that of a boy, aged 3 years, with active pulmonary tuberculosis and acute proteus bacillus otitis media and mastoiditis (the complete counts in this case are given in table 3). Case 18 (right) was that of a boy, aged 4 years, with acute hemolytic streptococcus otitis media. *F* indicates the probable first fever of the prodromal period; *K*, the appearance of Koplik's spots, and *R*, the appearance of the rash.

until the beginning of convalescence does it rise again to the normal level. In the composite analysis, lymphopenia is thus limited to, and constantly present during, the febrile period, and the variations of

greatest magnitude in the curve occur at the beginning and at the end of this period.

Consideration of the lymphocyte reactions in the individual cases brings out certain important features. A decrease in the number of lymphocytes on the first day of fever was observed in fourteen of the sixteen cases (figs. 4 to 8). In two cases it was delayed for twenty-four hours (case 5 and 6, fig. 6). Other peculiarities in the lymphocyte reaction were encountered in a few cases. In four of the children, following the typical fall in the number of lymphocytes on the first day, a sharp temporary increase in the count occurred (cases 7 and 9, figs. 7 and 8). The time of appearance of this increase was variable, but in each instance it was limited to one day. In three of the cases the rise in lymphocytes was coincident with a remission of the fever, a phenomenon that is characteristic of measles before the appearance of the eruption. Still another variety of response that has undoubtedly been a source of confusion is illustrated in case 10, in an infant of 9 months (fig. 8 and table 3). Here, because of a simultaneous drop in the polymorphonuclear cells, the lymphocyte percentages failed to indicate the development of a lymphopenia. The true nature of this reaction has been repeatedly obscured through the use of the term "relative lymphocytosis," a description of ambiguous import. Indeed, the occurrence of such instances of "relative lymphocytosis" has been cited as evidence of the great variability of the lymphocytic reaction in measles. That it is not the lymphocyte response that is responsible for the variability of the blood picture is, however, strikingly demonstrated when the blood counts are analyzed in terms of absolute numbers.

The counts in one case (case 11) that proved to be quite exceptional are given in table 3. In this instance, lymphopenia was observed three and four days before the onset of fever, and again on the first day of the febrile period. Following this the lymphocyte counts rose more or less steadily until convalescence was established.

It is of considerable interest that complicating infections did not interfere with the development of the typical lymphocyte reaction. Although the added illness was in some instances quite severe, a pronounced fall in the number of lymphocytes due to measles was regularly apparent. When the course was already febrile, as in the case of pyogenic infections, the lymphopenia occurred simultaneously with a sharp rise in fever, five days before the appearance of the rash (fig. 9). When the complicating illness was afebrile, as in the case of pulmonary tuberculosis (case 20, table 3), the drop in lymphocytes was observed on the first day of fever.

Pathologic Changes in Lymph Nodes: It has long been known that a progressive enlargement of the lymph nodes develops during the

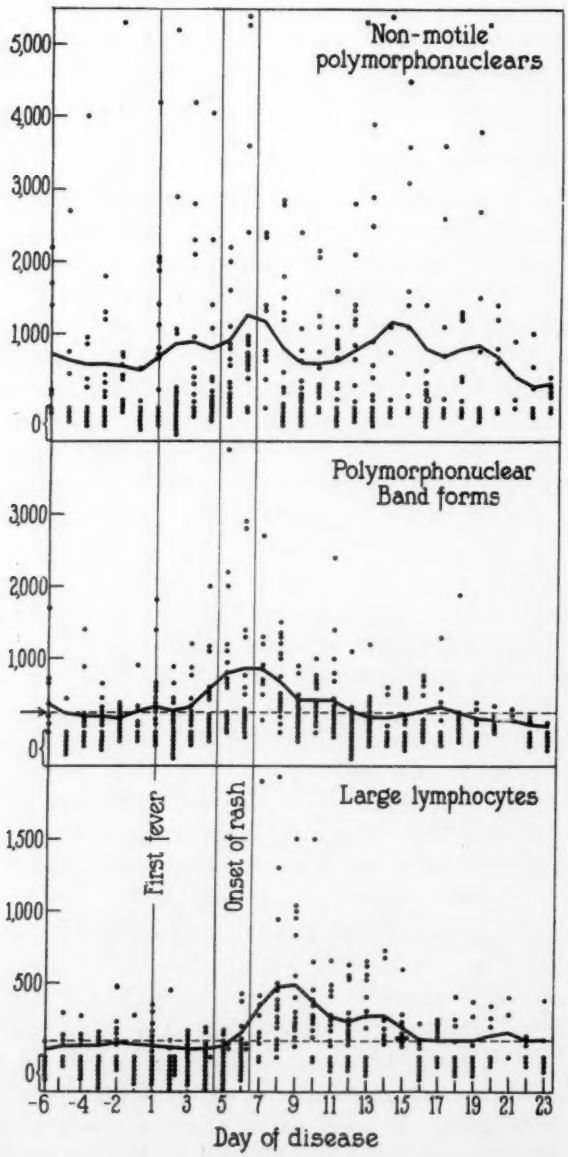

Fig. 10.—Reactions of nonmotile leukocytes, polymorphonuclear band forms and large lymphocytes during uncomplicated measles. The curves represent the averages of the blood counts in sixteen cases, the individual counts being plotted as separate points. The calculated normal level is shown in each instance by a broken line. *First fever* indicates the onset of the period of invasion.

febrile period of measles and reaches its height when the rash appears. The auricular, occipital and epitrochlear glands regularly become palpable, and a marked discrete enlargement of the cervical, axillary and inguinal nodes occurs. Ewing [25] and Denton,[26] in reporting their pathologic studies on measles, noted the presence of hyperplastic and inflammatory reactions in the lymph glands. It became of interest, therefore, in the course of the present study, to determine whether a more detailed investigation of the glandular enlargement would throw light on the lymphopenic reaction of the peripheral blood. The questions arose as to whether the changes in the nodes were predominantly of a degenerative nature as in yellow fever,[27] whether they were purely hyperplastic, or whether the reactions were more complex, consisting of varying degrees of necrosis, edema and hyperplasia, as in diphtheria,[28] smallpox,[28] scarlet fever,[28] poliomyelitis [29] and typhoid fever.[30] Accordingly, permission was obtained for taking a specimen for biopsy from a boy of 2 years (case 5, fig. 6) who had uncomplicated measles that ran a typical course. The most marked lymphopenia (900 cells) was present on the fourth day of fever, at which time the eruption appeared. On this day two posterior cervical nodes were removed, and examinations of supravital preparations as well as of fixed tissue sections of both glands were made.

Sections of the lymph nodes (figs. 11, 12 and 13) showed marked hyperplastic changes. Both the normal demarcations separating individual follicles and the more or less clear differentiation of the cortex from the medulla of the glands had in large measure disappeared. In the larger of the two glands this change resulted in an almost complete loss of normal architecture. The follicles and lymph cords were packed with lymphocytes of all sizes, and the tissue also showed a marked degree of active congestion with red blood cells. In the germinal centers the

25. Ewing, J.: The Epithelial Cell Changes in Measles, J. Infect. Dis. **6**:1 (Feb.) 1909.

26. Denton, J.: The Pathology of Fatal Measles, Am. J. M. Sc. **169**:531 (April) 1925.

27. Hudson, N. P.: The Pathology of Experimental Yellow Fever in the Macacus Rhesus: II. Microscopic Pathology, Am. J. Path. **4**:407 (Sept.) 1928; III. Comparison with the Pathology of Yellow Fever in Man, ibid. **4**:419 (Sept.) 1928.

28. Councilman, W. T.: Changes in the Lymphoid Tissue in Certain of the Infectious Diseases, Philadelphia, J. B. Lippincott Company, Harvey Lecture, 1908, p. 268. Councilman, W. T.; Magrath, G. B., and Brinckerhoff, W. R.: The Pathological Anatomy and Histology of Variola, J. M. Research **11**:12 (Feb.) 1904.

29. Peabody, F. W.; Draper, G., and Dochez, A. R.: A Clinical Study of Acute Poliomyelitis, Monograph 4, New York, Rockefeller Institute Medical Research, 1912, p. 1.

30. Mallory, F. B.: A Histological Study of Typhoid Fever, J. Exper. Med. **3**:611 (Nov.) 1898.

cells appeared to be normal (fig. 12). Nowhere was there evidence of necrosis or of exhaustion of these centers. Mitotic figures were numerous and appeared to be present chiefly in large wandering mononuclear cells. The medullary sinuses were widely distended and contained a great variety of mononuclear elements. In the peripheral

Fig. 11 (case 5).—Marked hyperplastic changes in a posterior cervical lymph node excised on the first day of the rash, when lymphopenia was most striking (fig. 6). Eosin and methylene blue (methylthionine chloride, U. S. P.) stain; × 40.

sinuses certain large cells with round or ovoid nuclei and with a considerable amount of deeply basophilic cytoplasm were particularly in evidence (fig. 13). Basophilic cells of similar appearance, which were found in large numbers in the patient's peripheral blood two days after

the glands were excised, are referred to in another section of the article. In the supravital preparations of the tissue, which were made immediately after the removal of the glands from the body, the most striking phenomenon was the presence of numerous young monocytes with very small neutral red rosettes around their centrospheres.

In a recent report, Warthin [31] described the pathologic changes in tonsils excised from patients during the prodromal period of measles. He noted the presence of large numbers of multinucleated giant cells in the germinal centers and in the subepithelial lymphoid tissue of the tonsils. He regarded this phenomenon as the essential pathologic change of measles in the upper part of the respiratory tract and believed that the etiologic agent of measles was phagocytosed by these giant cells. An attempt was made to determine whether this interesting observation of Warthin's in regard to the tonsils could be extended to the cervical lymph nodes. An examination of several sections, however, revealed only one giant cell. The significance of one such cell is questionable, especially in view of the fact that an occasional giant cell is present in normal lymph nodes.[32]

If, as appears probable from the foregoing observations, hyperplasia of lymphoid tissue is a characteristic reaction to the virus of measles, the existence of a decreased number of lymphocytes in the blood seems to indicate that the lymphocytes proliferate actively but fail for some reason to reach the general circulation.

Monocytes: No abrupt variation in the number of monocytes occurs on the first day of fever comparable to that which appears in the lymphocyte counts (fig. 3). Instead the monocytes continue to be present in high or normal numbers during the first three days of the febrile period. During the succeeding days of this period there is a rapid fall in the curve to a minimum on the sixth to eighth days, at which time most of the plotted monocyte counts are clumped between values of 0 and 500. The presence of a few scattered high monocyte counts at the time of the rash is nevertheless indicative of a considerable degree of variability in the reaction of these cells. Some of the high values are due to what Sabin has described as a "shower" of cells into the peripheral circulation. In case 1, for example, the monocyte count on the fifth day of fever was 1,800, while on the third, fourth, sixth and seventh days the counts ranged between 250 and 460. Aside from

31. Warthin, A. S.: Occurrence of Numerous Large Giant Cells in the Tonsils and Pharyngeal Mucosa in the Prodromal Stage of Measles: Report of Four Cases, Arch. Path. **11**:864 (June) 1931.

32. Drummond, W. B.: On the Structure and Functions of Haemolymph Glands, J. Anat. & Physiol. **34**:198 (Jan.) 1900. Forkner, C. E.: Material from Lymph Nodes: IV. The Heterology of Lymphoid Tissue with Special Reference to the Monocyte; Supravital Studies, J. Exper. Med. **49**:323 (Feb.) 1929.

such a response, which was observed in several instances, the majority of cases exhibited monocyte reactions that followed the average curve (cases 2, 7, 8 and 10, table 3).

The numerical changes in the monocytes in the presence of complicating infections were similar to those observed in the cases of uncomplicated measles (cases 17 and 20, table 3).

Interesting qualitative changes in the monocytes were also frequently noted during the febrile period. Cells undergoing division were repeatedly observed, and it was rather common to see some containing two nuclei. Young monocytes, moreover, were noted with a fair degree of regularity. In these, either a well defined small rosette of fine neutral red bodies occupied the region of the centrosphere, or red granules scattered through the cytoplasm were present in unusually small numbers. Minute mitochondria, quite different from those seen in the lymphocytes, were present in great numbers and were usually much more distinctly visible than in the older monocytes. The rather small eccentric nucleus, instead of appearing narrow and horseshoe-shaped as in the mature type, was full and round or oval. The cytoplasm was abundant and lacked the clarity characteristic of lymphocytes. The relation that such young and dividing forms in the peripheral blood stream bear to a possible increased activity of the monocytes in the hyperplastic lymph nodes is a matter for further investigation. "Stimulated" monocytes of the type seen in tuberculosis were not observed in the blood smears of any of the children. The finding of a typical clasmatocyte in the blood was likewise exceedingly rare.

Period of Convalescence.—Total White Blood Cells: The more or less complete reversal of the blood picture that takes place during convalescence from measles is reflected in the rising total white blood counts of this period (composite curve, fig. 1). On the ninth day the number of leukocytes begins to increase and passes the standard normal level two days later. After remaining elevated for several days, the curve falls again to the normal level.

Although the counts in each of the fourteen cases that remained uncomplicated rose significantly during convalescence, in four cases leukocytosis failed to develop. Of the ten that showed counts above normal, only one manifested a leukocytosis on more than two consecutive days (case 1, fig. 4). For the most part, the curves in the individual cases showed isolated peaks of leukocytosis that were repeated at irregular intervals between the second and fourteenth days of convalescence (cases 6 and 10, figs. 6 and 8), while in three cases leukocytosis occurred on but a single day (case 5, fig. 6). For the uncomplicated cases, the high blood counts ranged between 13,100 and 18,300.

Ten of the entire group of forty-six patients presented complicating infections during the period of convalescence from measles. In three,

the illness antedated the measles and persisted after the disappearance of the rash. Of the remaining seven, three had secondary bronchopneumonia, the infecting organism in two being pneumococcus group IV and in one, Streptococcus hemolyticus. The patient in the latter case, in which there was also an overwhelming septicemia, succumbed four days after onset of the rash. Acute otitis media developed in three other children; in two, the infection was caused by Streptococcus hemolyticus and was followed by the development of mastoiditis; from the third, large numbers of hemolytic staphylococcus colonies were obtained. One

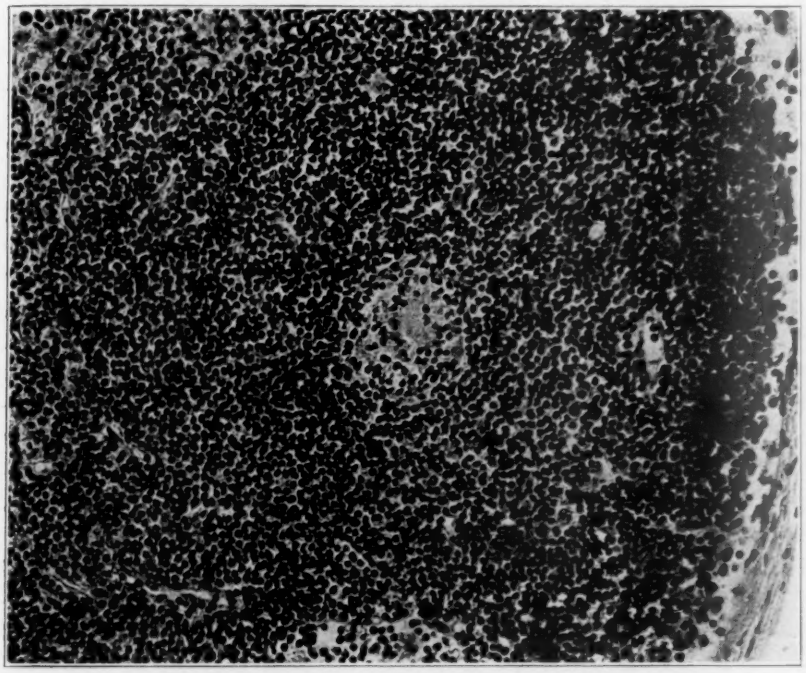

Fig. 12 (case 5).—Hyperplastic lymphoid follicle in a posterior cervical lymph node excised on the first day of the rash. There is no necrosis or exhaustion of the germinal center. Eosin and methylene blue stain; × 350.

patient showed pyuria following measles. Except for the patient with active tuberculosis and the child with sepsis, all the patients showed a leukocytosis during the convalescent period from measles. The degree of the leukocytosis, however, was not much more striking than that in the "normal" group, and in no case exceeded 22,500 (cases 7, 17 and 18, figs. 7 and 9, and case 20, table 3). It tended, furthermore, except in the cases of mastoiditis, to assume an irregularly fluctuating character similar to that seen in uncomplicated measles. The infant who died of a generalized hemolytic streptococcic infection showed a pro-

gressively falling white blood count, the leukocytes during the thirty-six hours prior to death dropping from 11,200 to 5,300.

Polymorphonuclear Neutrophils: Instead of immediately rising after defervescence, the number of polymorphonuclear neutrophils continues to diminish. Indeed, on the ninth day, a point corresponding in the majority of cases to the second day of convalescence, the neutrophils are at their lowest level (composite curve, figs. 1 and 2). This curious phenomenon, in which the most marked neutropenia follows the disease instead of accompanying it, was observed in all but two of the uncomplicated cases. After the preliminary fall, the neutrophil curve rises steadily to the level of moderate polymorphonucleosis at the end of the first week of convalescence. High values for the polymorphonuclear cells continue to be evident during most of the second week. Observations during the third week are limited to four cases, and in daily counts on these patients during this period, only normal numbers of neutrophils were encountered.

The presence of a considerable number of low charted values (fig. 2) is indicative of the inconstancy of the upward trend of the neutrophils. Two factors contributed to this irregularity. In the first place, polymorphonucleosis developed in only 50 per cent of the cases (case 2, table 3); in five cases the counts fluctuated entirely within normal limits (cases 4 and 8, table 3), and in two neutropenia was actually found (case 10, table 3). In the second place, when polymorphonucleosis occurred, it assumed a more or less fluctuating character similar to that of the total white blood count described; i. e., one or more isolated peaks of from 8,000 to 10,000 cells were followed by, or alternated with, counts in the neighborhood of 4,000.

As was to be expected, complicating pyogenic infections modified to some extent the typical reactions of the polymorphonuclear neutrophils. In the instances in which the pyogenic infections were present during both the febrile and the convalescent periods of measles (case 17, table 3), the curves of the neutrophils presented the same general shape as did those in the uncomplicated cases, but were constantly at a higher level. When the infection closely followed the measles, as in the cases of secondary pneumonia, the low levels for neutrophils on the eighth and ninth days were conspicuously absent (case 7, table 3). In the fatal case of sepsis, a progressive neutropenia developed toward the end. When the complicating infection appeared a number of days after the beginning of convalescence, the neutrophil reaction was similar to that in uncomplicated cases. In the cases of mastoiditis, however, the polymorphonuclear leukocytes eventually attained higher levels, 15,000 as compared with 10,000 in the cases without complications. Tuberculosis appeared to have no effect on the neutrophil reaction usually seen during convalescence from measles.

Polymorphonuclear Band Forms: Immediately following the febrile period, the curve of the band forms falls to the normal level (fig. 10). Moderately severe, acute pyogenic infections present during convalescence occasionally caused a second shift to the left in the polymorphonuclear group.

Eosinophils: Whereas on the seventh day of the febrile period of measles only two of the charted blood counts show eosinophils, the number of such counts is increased to eight on the following day (fig. 3). The latter day marks the beginning of convalescence in the majority of cases. On the second day of the convalescent period (day 9, fig. 3), thirteen of the fourteen counts are above the zero level. The curve rises rapidly during this period and reaches the average normal level within four days. It subsequently shows little tendency to exceed the normal, although several of the plotted points fall definitely within the range of eosinophilia. From an analysis of the eosinophil reactions in the individual cases, it was found that seven cases, in fact, manifested abnormally high eosinophil counts at irregular intervals during the two weeks following the measles (case 4, table 3). The remainder, however, merely showed a return to normal eosinophil values (cases 2, 8, 10 and 11, table 3).

Since the number of eosinophils is diminished in a variety of acute infections, it is to be anticipated that complications might delay the normal return of eosinophils into the peripheral blood at this stage. This proved to be so, particularly in the cases in which secondary pneumonia developed. Under such conditions the eosinophils did not reappear in the blood smears until the beginning of recovery from the pulmonary infection. Other complicating illnesses resulted in similar, though not so pronounced, deviations from the eosinophil response following uncomplicated measles. This inhibitory phenomenon was, nevertheless, not observed in all cases. When the complicating infection was mild or when it antedated the measles, the eosinophil reaction was frequently not very different from that in the simple cases (case 17, table 3). The patient with active tuberculosis (case 20, table 3) did not manifest the delayed reaction observed in the children with acute pyogenic complications.

Basophils: After four or five days of convalescence the basophil curve begins to rise and then mounts steadily to reach a peak at the end of the second week of this period (composite curve, fig. 3). It will be seen that the highest portion of the curve owes its elevation to the absence of zero basophil counts as well as to high values present at this time in individual cases. In spite of the element of uncertainty in basophil counts, the changes were observed with sufficient regularity (table 3) to suggest strongly that basophilia occurs during the second week of convalescence from measles.

Lymphocytes: At the end of the febrile period the curve of the lymphocytes (fig. 2) begins to rise sharply. On the second day of convalescence (day 9, figs. 1 and 2) it has in its ascent already passed the average normal level. Then follows a period of about five days during which the elevation of the curve indicates the development of a postfebrile lymphocytosis. During the second week of convalescence

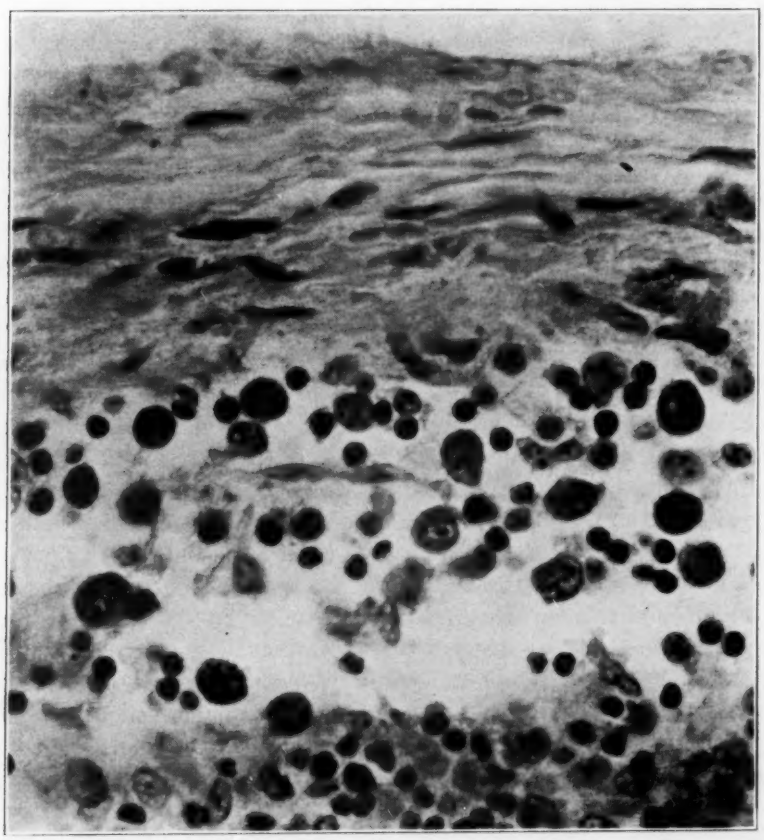

Fig. 13 (case 5).—Numerous large basophilic mononuclear cells in the peripheral sinus of a lymph node excised on the first day of the rash. Similar cells were not seen in the circulating blood until the beginning of convalescence, forty-eight hours later, at which time they constituted more than 15 per cent of the total lymphocytes. Eosin and methylene blue stain; × 750.

there is a fairly sharp fall in the curve followed by a slow return to the average normal level.

The counts in the individual cases manifested considerable uniformity in the development of the lymphocytic reactions just described. In all cases the lymphocytes showed marked increases early in convalescence.

and in nine of the fourteen children the rise attained the level of definite lymphocytosis (figs. 4 to 8). At the beginning of the second week of this period, on the other hand, high lymphocyte counts were not observed. Some cases, indeed, actually showed lymphopenia at this time (case 2, fig. 4, and case 4, table 3). During the third week all counts were again entirely normal.

With the development of convalescence the character of the lymphocytic group of cells is definitely modified. From figure 10 it is evident that there is a sharp rise in the number of large lymphocytes,[33] amounting to about a tenfold increase. The rise in the curve of large lymphocytes is, therefore, out of all proportion to the degree of lymphocytosis (composite curve, fig. 1). Furthermore, it will be seen that the maximum elevation of the large lymphocytes precedes by one or two days the high level attained by the lymphocyte group as a whole.

The alteration in the percentages of the different types of lymphocytes was accompanied by a change in the appearance of the individual cells detectable both in supravital and in fixed preparations. In the living state, the most striking qualitative changes were seen in the large lymphocytes, although they were frequently observed in the intermediate forms and occasionally in the small lymphocytes. The mitochondria increased in number and stained more intensely with Janus green (fig. 14). Possibly because of the intense staining reaction, these cytoplasmic elements appeared to be larger than normal. Occasionally in such unusual cells a yellowish tinge to the protoplasm was observed. In some instances, a few rather large neutral red vacuoles were present in the cytoplasm. During the latter part of this period of lymphocytosis these abnormal cells rapidly diminished in number and were replaced by others manifesting characteristics transitional between the "large green mitochondrial types" and the ordinary lymphocytes. In preparations stained according to Wright's method cytologic differences could be distinguished with greater certainty. A most pronounced basophilic reaction of the cytoplasm was noted in the lymphocytes, particularly during the early part of the lymphocytosis. This change was obvious in some of the smaller lymphocytes as well as in the abnormally large ones. One of the large cells is illustrated in figure 15. It will be seen that the basophilic cytoplasm has a coarsely granular instead of a

33. It should be borne in mind that whereas most of the large lymphocytes in fixed preparations represent older forms, the cells that appear as large lymphocytes in supravitally stained blood films are younger. Cf. Wiseman, B. K.: Criteria of the Age of Lymphocytes in the Peripheral Blood, J. Exper. Med. **54**:271 (Aug.) 1931.

ground-glass appearance. Moreover, the evenly stippled appearance of the chromatin in the nucleus gives no suggestion of the presence of a "cart-wheel" pattern.

A number of authors have noted the appearance of such cells in the blood during convalescence from measles. In early reports, Reckzeh [1f] and Erben [1g] referred to an increase of large lymphocytes, but did not describe them in detail. A few years later, Hildebrandt and Thomas [34] reported the presence of Türk cells in one case. This observation has been confirmed by Lane.[35] Recently Usbeck [5a] and others [36] described the cells in question as plasma cells, while Bunting and Thewlis [37] expressed the belief that they are "capillary endothelial" cells.

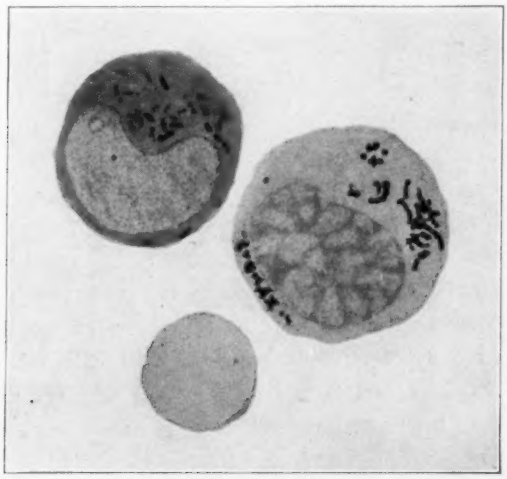

Fig. 14 (case 16).—Large lymphocytes found in the blood during convalescence from measles. The cell on the right, with the more brightly staining mitochondria, is typical of the young lymphocytes that appear at this time. A red cell is shown for comparative size. The differences in the appearance of the nuclei are the result of beginning degeneration of the preparation. (Photograph of a colored drawing by Louis Schmidt.) Supravital neutral red and Janus green stain, single microscopic field; × 1,700.

The presence of large basophilic cells in the blood stream is by no means peculiar to measles. In supravital preparations of the blood in

34. Hildebrandt, W., and Thomas, K.: Das Verhalten der Leukozyten bei Röteln, Ztschr. f. klin. Med. **59**:444, 1906.

35. Lane, H. A.: The Blood Picture in Measles, Brit. M. J. **1**:950 (May 24) 1930.

36. Redlich, F., and Maternowska, Z.: Beitrag zur Hämatologie der Masern, Monatschr. f. Kinderh. **38**:178 (Jan.-Feb.) 1928.

37. Bunting, C. H., and Thewlis, E.: Leukocytic Reactions in Smallpox, Chickenpox, Scarlet Fever, Measles and Mumps, Arch. Path. **1**:189 (Feb.) 1926.

two other diseases associated with clinical evidence of lymphoid hyperplasia, viz., infectious mononucleosis [38] and German measles,[38] we have observed the presence of cells identical in appearance with those described for measles. That such cells in the blood have their origin in the lymph nodes seems fairly certain because of the earlier presence of large numbers of similar cells in the sinuses of the glands (fig. 13). That they are young lymphocytes and not plasma cells also seems most probable in view of Miller's [39] studies on the life cycle of the plasma cell. Neither in supravital preparations nor in the sections of lymph nodes do the large basophilic cells of measles appear to correspond exactly to any of the stages in the development or degeneration of plasma cells.

Fig. 15 (case 16).—Lymphocytes found in the blood during convalescence from measles. The cell on the right, with deeply basophilic cytoplasm, is typical of the young lymphocytes as they appear in fixed blood films. The majority of these cells, however, are not vacuolated as is the one pictured. (Photograph of a colored drawing by Louis Schmidt.) Wright's stain, single microscopic field; × 1,700.

On the other hand, they closely resemble the young lymphocytes described in a recent study by Wiseman.[33]

38. The increase of basophilic mononuclear cells in fixed blood smears from these conditions is well known. Cf. Sprunt, T. P., and Evans, F. A.: Mononuclear Leucocytosis in Reaction to Acute Infections ("Infectious Mononucleosis"), Bull. Johns Hopkins Hosp. **31**:410 (Nov.) 1920. Naegeli, Otto: Blutkrankheiten und Blutdiagnostik: Lehrbuch der klinischen Hämatologie, ed. 5, Berlin, Julius Springer, 1931, p. 619.

39. Miller, F. R.: The Induced Development and Histogenesis of Plasma Cells, J. Exper. Med. **54**:333 (Sept.) 1931.

Two facts of interest are brought out in a consideration of the lymphocytic reactions in complicated cases. Although the development of the lymphocytosis after measles might have been delayed, as it was in one patient with pneumonia (case 7, fig. 7), with one exception a pronounced increase in the lymphocyte count nevertheless occurred in every case (fig. 9 and case 20, table 3). In the exceptional case, the development of fatal sepsis was accompanied by a progressive lymphopenia, the lymphocyte count falling to 1,000 on the day before death. Even in this case, there was an increase in the number of large young lymphocytes, the last count, taken three days after the onset of the rash, revealing 530 large cells, more than half of the total lymphocytes present.

Monocytes: At the time of the onset of convalescence the monocyte curve rises sharply and reaches the normal level on the third day of this period (fig. 3). It remains at this level until the end of the first week, at which time it rises well above normal. Toward the latter part of the second week the curve falls again to the standard average level, and thereafter normal values are maintained.

Despite the fact that the charts of individual cases show frequent fluctuations with the appearance of low counts at intervals during convalescence, only one patient failed to manifest an elevation in the monocyte curve during this period. In several of the cases fluctuations were only minimal, and the resulting monocyte curve followed the typical average curve quite closely (cases 8 and 10, table 3).

Complicating illnesses appeared to exert very little effect on the monocyte reaction. In both the pyogenic and the tuberculous cases, monocytosis or at least increased numbers of monocytes appeared in the blood at the expected time (cases 7, 17 and 20, table 3).

COMMENT

From the data presented in this paper it is evident that infection with measles causes profound changes in the blood involving all of the leukocytic elements. While the predominant reaction of each of the cell types is one of numerical diminution during the height of the disease, important differences are noted, particularly in the time when the response of each kind of cell occurs (composite analysis, fig. 1). This is especially noticeable at the beginning of the febrile period when the first of the leukopenic changes is manifested by a sharp decrease in the number of lymphocytes and eosinophils. In contrast to this initial fall in the number of lymphocytes and eosinophils is the increase in the number of monocytes and polymorphonuclear neutrophils, which maintains the normal value for the total white blood count. Moreover, the period of most marked leukopenia of each of the different cellular elements is variable in its relation to the course of the disease. Thus, although

the lymphocytes fall to their lowest point before the onset of the rash, the monocytes are lowest at the end of the febrile period, while the most pronounced fall in the neutrophils does not occur until still later during convalescence. The eosinophils and basophils manifest an intermediate type of response, being most diminished at the time of appearance of the rash (figs. 1 and 3). The "shift to the left" phenomenon also varies in regard to the time of its appearance in the different cell groups. Among the polymorphonuclear neutrophils and the monocytes, for example, the greatest number of young forms is seen during the eruptive phase of measles. Among the lymphocytes, however, young types are seen in great abundance only during the early period of convalescence.

Regarding the uniformity of the leukocytic response, it is, of course, obvious that deviations from a fixed pattern are to be found just as commonly as in other biologic phenomena. The instances of failure to conform to type, however, usually reveal themselves as minor variations rather than as fundamental differences of reaction. Thus, it is true that certain peculiarities in the cell counts, such as transient lymphocytosis during the prodromal stage, were observed in some cases. Nevertheless, it is apparent that the more persistent lymphopenia that developed during the febrile period in these very cases was quite as striking as it was in the more typical instances. Moreover, it is worthy of note that the general types of reaction described occurred in adults as well as in infants and children (table 3).

In view of the regularity with which typical leukocytic alterations are detected during measles, it is of interest to determine to what extent these changes are peculiar to this infection. Since the possible quantitative and qualitative changes that may occur in the white cells during different infections are apparently quite limited, it is usually unjustifiable to regard any leukocytic response as specific. It is not surprising, therefore, to find that leukopenic changes, corresponding more or less to those seen in measles, occur in a variety of diseases, particularly those caused by viruses and Rickettsias. Thus, simultaneous neutropenia and lymphopenia accompany the early phases of varicella, smallpox, yellow fever, psittacosis, dengue, typhus fever and other infections.[40] In some diseases, as in yellow fever, the reduction of the polymorphonuclear leukocytes is more striking than is the lymphopenia, while in other maladies,

40. Bunting and Thewlis (footnote 37). Berry, G. P., and Kitchen, S. F.: Yellow Fever Accidentally Contracted in the Laboratory: A Study of Seven Cases, Am. J. Trop. Med. **11**:365 (Nov.) 1931. Rivers, T. M.; Benjamin, B., and Berry, G. P.: Psittacosis: Report of a Case, J. A. M. A. **95**:577 (Aug. 23) 1930. Simmons, J. S.; St. John, J. H., and Reynolds, F. H. K.: Experimental Studies of Dengue, Philippine J. Sc. **44**:1 (Jan.-Feb.) 1931. Kossovitch, N.: Le sang dans le typhus exanthématique, Compt. rend. Soc. de biol. **93**:900 (Oct. 17) 1925.

as in psittacosis, the reverse is the case. Lymphopenia, moreover, is not limited to these groups of diseases. It is known to be present in severe pyogenic infections, and a recent study by Arany [41] indicates that a fall in lymphocytes occurs at the time of the initial fever of tuberculosis.

It is of interest, also, in this connection to compare the type of lymphocytosis following measles with that occurring after other diseases. It has been pointed out that a great outpouring of large young lymphocytes into the peripheral blood occurs early in convalescence from measles. This, however, is not true of all the lymphocytoses developing during recovery from different lymphopenic diseases. For example, in supravital preparations of the blood made at the time when the lymphocytosis following psittacosis and typhus fever occurred, we observed that large young lymphocytes were present only in very small numbers if at all. Kitchen [42] has made a similar observation regarding yellow fever. A possible explanation for the difference in these reactions is suggested by the pathologic changes noted in the lymphoid tissue of patients with yellow fever. Instead of the hyperplasia seen in measles, there is found a diminution of lymphoid tissue with necrosis and phagocytosis in the germinal centers.[27] Accordingly, when recovery from such an infection ensues, the development of lymphocytosis is much more gradual and lacks the pronounced shift to the left seen in measles.

It is thus evident that while a certain type of leukocyte response in the peripheral blood, e. g., lymphopenia, may be present in a variety of diseases, it does not necessarily follow that it always arises as the result of similar pathologic processes. Lymphopenia may be present in measles, rubella or infectious mononucleosis at a time when there is evidence of an increased production of lymphocytes in the tissues. The reasons for the delayed entrance of the lymphocytes into the blood stream in these conditions are not apparent. In certain instances, as in yellow fever, the low lymphocyte count may be indicative of a lack of normal production of these cells and of lymphocyte destruction. In other diseases, combinations of factors, such as cell destruction together with delayed entrance into the circulation despite hyperplastic changes, may be responsible for the fall in the lymphocytes of the blood. The pathologic and hematologic features of smallpox suggest that it falls into the latter class.

In view of the fact that the leukocytic reactions during measles are not unique, it might at first appear that blood counts are of little assistance in the early diagnosis of measles. Nevertheless, such a con-

41. Arany, L.: Das Blutbild beim tuberkulösen Initialfieber, Monatschr. f. Kinderh. **48**:492 (Dec.) 1930.

42. Kitchen, S. F.: Personal communication to the authors.

clusion is probably not warranted. The onset of the prodromal period of measles is rather peculiar in that the patient manifests fever, often of quite marked degree, with little other evidence of illness. At the same time the blood picture undergoes a pronounced change that is quite out of proportion to the clinically mild appearance of the infection. Under such circumstances, one should always consider the possibility that the fever is a sign of measles.

Little or no information regarding the prognosis of measles is gained by white blood cell counts. A marked shift to the left in the neutrophil group during the eruptive phase of the disease does not necessarily indicate an unusually severe illness. Similarly, the eosinophils may disappear early or late, or the number of lymphocytes, polymorphonuclear leukocytes or monocytes may fall to a surprising degree in clinically mild as well as in severe forms of the disease. Furthermore, in our group of cases, the onset of complications was not detected earlier by means of blood counts than by clinical examinations.

SUMMARY

The results of a study of the leukocytic reactions in forty-six cases of measles, including observations on twenty cases during the incubation period, are presented. The supravital technic was employed in making the counts, and in their analysis use was made of a table of normal values for each of the white cell elements during the different ages of childhood.

During the incubation period of measles, variations in the numbers of leukocytes are relatively slight. On the first day of the prodromal stage the leukocytic picture undergoes a striking alteration manifested principally by a fall in the number of lymphocytes. At the height of the disease all of the cell elements contribute to the production of leukopenia.

Histologic changes observed in lymph nodes obtained from one of the patients indicate that the development of the lymphopenia in measles is coincident with marked hyperplasia of the lymphoid tissues. Nevertheless, the young lymphocytes in the glands do not appear in great numbers in the blood stream until the beginning of convalescence.

Attention is directed to the possibility that the blood picture may be suggestive of measles at a time when fever is the only apparent clinical abnormality.

Dr. F. R. Sabin and Dr. C. A. Doan made many suggestions during the course of this study.

ACUTE INTESTINAL INTOXICATION ASSOCIATED WITH MASTOIDITIS IN INFANTS

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AND
WALLACE B. SMITH, M.D.
SAN FRANCISCO

In the past two years seven cases of mastoiditis in infants under 2 months of age have come under our observation. Reports of similar cases have been rather frequent in recent years, so they of necessity bear a marked similarity to our reports, but we hope by additional observation not only to substantiate what others have reported but to prove that encapsulated pus in the mastoid antrums of infants can cause a general metabolic disturbance, and that if drainage is instituted in time this toxemia can be corrected.

It was duVerney [1] of Paris, who, in 1684, during the reign of the Great Louis, left the first record of pathology. His record was a report of postmortem observations; it is only a few lines telling of extraneous material in the middle ear and mastoid. Tröltsch,[2] who began to write in the late 1850's, knew of duVerney's observations and complained of the inability to diagnose during life the conditions of the infant mastoid found at autopsy. It was principally through Tröltsch's influence, as well as Politzer's, that modern otology grew, developed and blossomed into its full maturity in German-speaking countries.

Otology developed rapidly during these years, and, while occasional attention was given the infant mastoid by different authors as the decades went by, it remained for Hartmann [3] of Berlin, in 1898, to raise the first question regarding the influence of infection of the mastoid on the gastro-intestinal tract in children. He believed infection to be the cause of severe metabolic disturbance and reported beneficial results from paracentesis.

Preysing,[4] in 1904, published an article reporting the result of bacteriologic and pathologic studies of the petrous bone in a hundred

1. du Verney, cited by von Tröltsch.[2]

2. von Tröltsch, A. F.: Lehrbuch der Ohrenheilkunde, ed. 7, Leipzig, F. C. W. Vogel, 1881, footnote, p. 436.

3. Hartmann, A.: Die Einwirkung der Otitis media der Säuglinge auf den Verdauungsapparat, Ztschr. f. Ohenh. **34**:1, 1898.

4. Preysing, Hermann: Otitis Media der Säuglinge. Bacteriologische und anatomische Studien, Wiesbaden, J. F. Bergmann, 1904.

postmortem examinations of infants. Of these infants—who had died from various causes—forty-six were reported as having died of gastro-enteritis. The pathologic findings showed that the change was principally in the mucous membrane, the bone not being markedly involved. There was engorgement of the whole petrous bone, as well as of the mucous membrane of the middle ear and of the membrane lining the antrum and the mastoid cells. Preysing concluded that the infection in the middle ear and mastoid caused gastro-intestinal disturbance, not because of inflammation of the intestinal mucosa by the exciting organism of the otitis, but because of absorption and transmission of toxins by the blood stream.

In 1921, Renaud [5] published an article which agreed with Preysing's pathologic findings in seventy autopsies. As a result of these examinations, and in an attempt to save some of the babies, postauricular drainage was attempted in the next ten cases. The high mortality of 87 per cent was attributed to the fact that operation was done too late—after the baby was in a desperate condition.

The substance of Marriott's [6] paper, read at the Washington meeting of the American Pediatric Society, in 1925, and the work of the group associated with him in St. Louis, including Alden and Lyman,[7] are too well known to warrant further review. These authors brought the clinical picture and the probable cause of the condition to the attention of the medical profession in such a way as to focus the attention of both the pediatrician and the otologist. As far as America is concerned, they launched the theory, although they did not add any new clinical data.

Since 1925 excellent articles have been published, such as those by Byfield,[8] Floyd,[9] McDougal and Knauer,[10] Coates,[11] McMahon [12] and

5. Renaud, Maurice: Unsuspected Otitis in Infants, Bull. et mém. Soc. méd. d. hôp. de Paris **15**:1325, 1326 and 1384, 1921; translated by Alden and Lyman: Laryngoscope (Aug.) 1925.

6. Marriott, McK.: Further Observations Concerning the Nature of Nutritional Disturbances, read before The American Pediatric Society, Washington, D. C., May 5, 1925, Laryngoscope **35**:592 (Aug.) 1925.

7. Alden, A. M., and Lyman, H. W.: Mastoid Infection in Infants, Laryngoscope **35**:586 (Aug.) 1925.

8. Byfield, A. H.: Systemic Effects of Chronic Infection in the Upper Respiratory Tract, in Abt, Isaac A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 3, p. 786.

9. Floyd, M. L.: Masked Mastoiditis Simulating "Alimentary Intoxication" (Anhydremia), Arch. Otolaryng. **1**:411 (April) 1925.

10. McDougal, J. J. C., and Knauer, W. J.: Five Atypical Cases of Mastoiditis in Children, Laryngoscope **33**:936, 1923.

11. Coates, G. M.: Mastoid Infection in Infants, Ann. Otol., Rhin. & Laryng. **36**:913 (Dec.) 1927.

12. McMahon, B. J.: The Pathology of Mastoiditis in Infants, Arch. Otolaryng. **7**:13 (Jan.) 1928.

the late Dr. Florence Holsclaw [13] of San Francisco. Opinion is divided as to whether infection in the mastoid is the cause of acute intestinal intoxication in infants. Four articles published in 1930 show clearly that all do not agree on the association of infection of the mastoid with the picture of severe gastro-intestinal intoxication and dehydration. These articles are of wide geographic distribution. Those by Carmack [14] of Indianapolis and Champion [15] of San Antonio affirm the relationship, while those of Wishart [16] of Toronto and Helwig and Dixon [17] of Kansas City deny any association. Our cases will not add anything new clinically, but we feel that a better acumen in diagnosis has been developed, owing to a more understanding cooperation between the departments of pediatrics and otology. That, together with a promptness in the application of remedial measures, has made it possible to report only a 17 per cent mortality in a series of six cases in which operation has been performed.

AUTHORS' EXPERIENCE

These cases have arisen among infants being cared for by an organization in San Francisco known as the Babies' Aid. It is under the auspices of the Associated Charities, and about two hundred tiny babies pass through the institution each year. Dr. Florence Holsclaw, in 1930, reported a series of similar cases occurring in the institution. It is unusually significant that this type of case is usually found in institutionalized babies and seldom in private practice. It has been claimed that the former high mortality was due to the lack of resistance in this class of motherless babies. Most of the infants were born of normal parents in the wards of the various San Francisco hospitals. After being admitted to the Babies' Aid, they have the optimum amount of violet rays and sunshine. Six graduate nurses attend them, and a physician visits them daily, so that lowered resistance, as maintained by some, can scarcely be a factor. We suggest that the reason for this high incidence of mastoiditis in institutionalized babies is not their lack of resistance but the fact that they are not handled so much as private

13. Holsclaw, F. M.; Boehm, C. A., and Bierman, J. M.: Otitis Media and Mastoiditis in Infants Under Three Months of Age, Am. J. Dis. Child. **39**:74 (April) 1930.

14. Carmack, John W.: Mastoiditis with Gastro-Intestinal Disturbance in Infants, Ann. Otol., Rhin. & Laryng. **39**:75 (March) 1930.

15. Champion, A. N.: Otitis and Nutritional Disorders in Infancy, Texas State J. Med. **26**:31 (May) 1930.

16. Wishart, D. E. S.: Relations of Infection of Ear and of Intestinal Tract in Infants, J. A. M. A. **95**:1084 (Oct. 11) 1930.

17. Helwig, F. G., and Dixon, O. J.: The Frequency of Mastoiditis in Infants, Arch. Otolaryng. **11**:169 (Feb.) 1930.

patients in the home. The latter baby with an infection of the upper respiratory tract is constantly being picked up or in an adult's arms, so that the discharges are allowed to drain into the nasopharynx and to be swallowed, whereas the institutional baby with rhinitis must of necessity lie quietly most of the day. The nasal discharges thus accumulate and lie against the mouth of the eustachian tube, thereby allowing the infection to travel up to the middle ear.

It is significant that Dr. Holsclaw's report shows that pneumonia was found in nine of sixteen fatal cases. It consequently occurred to us that the strictest care should be taken in keeping the room at a constant temperature. Besides this precaution, our babies with an infection of the upper respiratory tract were always laid on their abdomens and were picked up as often as possible, to facilitate drainage of nasal discharges. In addition to these precautions, we have performed operations in an improvised operating room at the Aid rather than transfer the children to the Children's Hospital, which is a distance of 2 miles. We are reporting a series of six cases in which an operation was performed and one other case the diagnosis of which was made at autopsy.

Four of the seven cases were the result of epidemics of diseases of the upper respiratory tract which swept through the wards, but, because of the strict care taken in observing the aforementioned precautions, in only four of thirty-seven patients did mastoiditis develop. The remaining three patients were babies who on admission to the Aid were found to have nasopharyngitis. In this series an infection of the upper respiratory tract invariably preceded the operation on the mastoid by from eight to fourteen days. Thus, clinically at least, we feel that mastoiditis is the end-result of an acute infection of the upper respiratory tract. The gastro-intestinal symptoms always begin with the onset of the nasopharyngitis, but the profound toxemia occurs only with the development of the mastoiditis.

The typical picture was shown by normal babies who suddenly refused the bottle; within from twenty-four to forty-eight hours the stools increased to six or eight a day. These were loose, with some mucus, but they were not watery. On examination either acute rhinitis or a reddened nasopharynx was found. In spite of local nasal applications and an indicated change in formula, the symptoms continued. Because of this progression of symptoms the otologist was called in at this point. Often nothing more than a slightly reddened drum or an absent light reflex was found, but because of the history the drums were usually opened, the result being either frank pus, a drop of serum or a dry tap. The result of the puncture, however, seemed to be no indication as to whether or not we were dealing with a case in which mastoiditis

Cases of Mastoiditis in Which Operation Was Performed

	Name	Age, Weeks	Weight	Wassermann	Temperature	Time Relation of Predisposing Disease to Date of Operation, Days	Clinical Course and Symptoms	Course of Aural Condition: Right	Course of Aural Condition: Left	Operation: Right	Operation: Left	Organism: Right	Organism: Left	Result
1	E. S.	7	8 lbs.	—	99°	8	Nasopharyngitis nasal discharge, cough, poor appetite, loose stools (4-5)							
						3	Otitis media Watery diarrhea, acute dehydration, cyanosis, toxemia	Loss of light reflex Paracentesis, serous discharge	Reddened drum	Bilateral mastoidectomy		Strep. viridans	Staph. albus	Recovery
2	B. P.	7	6 lbs., 7 oz.	—	99°	15	Stomatitis and thrush							
						7	Nasopharyngitis Loss of appetite, distention, diarrhea							
					103°	3	Otitis media Acute dehydration, loss of weight, toxemia	Reddened drum Paracentesis, pus in both antra	Bulging drum	Bilateral mastoidectomy, stringy pus in both antrums		Strep. viridans	Staph. aureus	Recovery
3	L. C.	3	7 lbs.	—			Bad feeder from birth							
					92.2°	6	Rhinitis Loss of appetite, acute loss of weight, slight diarrhea							
					101°	2	Otitis media Watery diarrhea, distention, occasional vomiting, dehydration, cyanosis	Drum normal Paracentesis, no discharge	Drum normal	Bilateral mastoidectomy, left antrum, stringy pus, right —no pus		Staph. aureus	Staph. aureus	Recovery
4	E. K.	3½	7 lbs., 6 oz.	—	100.2°	9	Rhinitis and nasopharyngitis Loss of appetite, loose stools (6)							
						7	Otitis media—right Watery diarrhea (10-15) distress, gas	Drum bulging, paracentesis, pus discharge	Drum normal					
					103°	2	Otitis media—left Acute loss of weight, watery diarrhea, no vomiting, dehydration, cyanosis, looked gray, toxemia		Absent light reflex, paracentesis, pus discharge	Bilateral mastoidectomy, small, mastoid cells found Pus	Pus	No growth aureus	Staph. aureus	Recovery
5	B. K.	5	8 lbs., 2 oz.	—	98°	17	Rhinitis and spasmodic bronchitis							

5	B. K.	5	8 lbs., 2 oz.	—	98°	17	Rhinitis and spasmodic bronchitis Looked gray, no diarrhea						
						14	Bronchopneumonia Diarrhea, cyanosis, persisting vomiting						
						4	Otitis media (1st ear) Dehydration, diarrhea, vomiting, distention, prostration	Reddened drum	Normal drum Paracentesis, pus obtained both ears				
					101.4°	2	Otitis media (2nd ear) Toxemia		Stopped draining, opened second time				
										Bilateral mastoidectomy, normal antrum Membrane thickened, pus	No growth	B. coli	Recovery
6	Y. H.	3	4 lbs., 12 oz.	—	99°	10	Rhinitis and nasopharyngitis Distention, diarrhea (5-6), loss of appetite						
						4	Bronchitis Diarrhea (8), vomiting						
					102°	2	Lobar pneumonia Diarrhea, vomiting, distention						
					103°	1	Otitis media Prostration, dehydration, acute toxemia	Reddened drum	Absent light reflex Paracentesis, no discharge				
										Bilateral mastoidectomy Stringy pus Pus	B. coli	B. coli	Died
Case of Mastoiditis in Which No Operation Was Performed													
7	B. G.	6	7 lbs., 14 oz.	—	100°	14	Nasopharyngitis Loss of appetite, acute diarrhea, toxemia						
						9	Otitis media Diarrhea, prostration, dehydration, toxemia	Reddened drum Pus	Loss of light reflex Paracentesis Pus				
					102°	4	Parotitis Toxemia, no appetite, drainage of pus from Stenson's duct		Gland incised one day before death, one oz. pus obtained				
										Autopsy, mastoiditis Stringy pus Neg.	Strep.	No growth	Died

was to develop. From this point on, in the patient in whom a mastoiditis developed, toxemia and dehydration rapidly appeared. The diarrhea became progressively worse, the stools numbering from ten to twenty a day. These became more watery, with small particles of undigested food and a large proportion of glairy mucus. Dehydration became marked, regardless of physiologic solution of sodium chloride given intraperitoneally once or twice a day, the loss of weight often being from 4 to 12 ounces (113 to 340 Gm.) a day. The baby became lethargic and cried but seldom, and then only with a weak and subdued cry. He lost all interest in his food, taking but a few ounces a day, and that only after being urged. The face became expressionless. Finally there was a pinched look about the nose and a slight cyanosis around the mouth. Altogether, he presented a gray appearance. There was always vomiting to a greater or less extent, although it never seemed one of the outstanding symptoms. The temperature was seldom more than 101 F. rectally. It was at this period—from eight to fourteen days after the onset of the symptoms—that we instituted postauricular drainage, not because of any positive local signs, but because of a recent history of infection of the upper respiratory tract and an acute intoxication which would respond to none of the remedial methods.

One of our cases illustrates this succession of events excellently. The infant contracted a severe infection of the upper respiratory tract. Moderate diarrhea was the only gastro-intestinal symptom for three days. Then, as the infection developed into bronchopneumonia, vomiting was added to the picture. At the end of ten days, regardless of the fact that the chest was absolutely clear, the baby became suddenly worse, with the picture of severe toxemia and dehydration. At operation on the seventeenth day pus was found in both mastoid antrums, from cultures of which B. coli was grown. We are of the opinion that mastoiditis developed during the course of the pneumonia, when the patient, in the act of vomiting, forced duodenal contents through the eustachian tube into the middle ear.

The other patient in whom we found colon bacilli was a 4½ pound (3,000 Gm.) premature baby of 5 weeks, with almost the same history—a reddened nasopharynx six days before lobar pneumonia developed. During the course of the pneumonia vomiting became frequent and forceful. On the ninth day, as the pneumonia was abating, the toxemia increased. The mastoid was opened on the tenth day, and pus containing B. coli was found in both antrums. This was the only patient lost of the six on whom we operated.

In the typical case in which pneumonia is not a complicating factor we reiterate that vomiting is not a marked symptom. We feel that in our five other patients the infection was introduced into the middle ear by mucopurulent discharges that had accumulated at the mouth of

the eustachian tube during the nasopharyngitis. Therefore, our bacterial growth in the mastoid varied with the kind of discharge that gained entrance into the middle ear and antrum. It is coincident with this mastoid infection that the profound picture of toxemia and dehydration is precipitated.

In each of these seven patients pus was found in the mastoid antrum, and in two patients small infected cells were also found. The organism varied. Streptococci were found in three patients, Staphylococcus aureus in four, Staphylococcus albus in one and B. coli in three; no growth on culture was reported in two cases.

Contrary to other writers, we feel that the kind of organism does not vary the clinical picture. The toxemia, we think, is due to the encapsulated pus. Although paracentesis was always done, drainage did not always result, probably owing to the fact that in the first few weeks of life the lining of the antrum lies in thick, mesodermal folds, which, when infected, swell so that the antrum is entirely separated from the middle ear.

The operation in infants at this age is a simple procedure. In all of our cases it was done under local anesthesia, with 0.5 per cent procaine hydrochloride. An incision of only 2 cm. is required to expose the periosteum above the superior bony wall of the external auditory canal. With a small curet the mastoid antrum is uncovered. This usually consists of a single cell, but in two of our patients other small mastoid cells were found. The granulations are carefully curetted, and a small drain placed in the mastoid. The incision is left open.

The shock is minimal in the hands of a careful operator. This is evidenced by the definite improvement that is seen in these babies after twenty-four hours. To appreciate this change one must realize how seriously ill an infant of 6 weeks can become after a depleting sickness of from eight to fourteen days; consequently any procedure that results in an entirely different picture after forty-eight hours must of necessity have obviated the offending factor.

Our mortality statistics do not prove the cause of intestinal intoxication in infants to be mastoiditis, but since keen interest has been taken in these infants by the otologists, with subsequent postauricular drainage done when necessary, and since we have performed our operations in the same room in which the infant was kept, eliminating the necessity of taking a very sick young baby from a warm room through the fog to the Children's Hospital, mortality statistics have dropped from 6.3 per cent in 1925 and 1.8 per cent in 1929 to 0.6 per cent in 1930.

SUMMARY

1. Five of six babies recovered from an acute intestinal intoxication after postauricular drainage was instituted.

2. From clinical observations we feel that mastoiditis develops in the course of an infection of the upper respiratory tract, but it is only with the onset of the mastoid infection that the profound toxemia develops.

3. Regardless of the kind of organism found in the mastoid antrum, our clinical picture did not vary.

It is through the courtesy of Drs. Rae Ashley and A. G. Rawlins that we are reporting cases 5 and 7.

SUPPURATIVE PLEURITIS IN CHILDREN

ITS PATHOGENESIS, DIAGNOSIS AND TREATMENT

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Infections of the pleura in infants and young children present many problems that differ materially from those encountered in adults. For this reason we have given separate consideration for a number of years to the subject of empyema in children, and have gradually evolved a plan of treatment based on the following features: (1) the clinical picture, (2) the nature of the pathologic process and (3) the bacteriology. All three aspects will receive consideration in this paper, and the operative treatment to be described will be based on them.

The term "pleural empyema" is obviously an all-inclusive one, and has no meaning other than to denote pus in the pleural space. Its significance, unless qualified, is as obscure as the term "peritonitis." The answer to the question, "What is the correct treatment for empyema?" can be given only as intelligently as to a similar inquiry concerning peritonitis. We shall employ terms descriptive of the pathologic and bacteriologic nature of the pleural infection, for example, diffuse streptococcic pyothorax and encapsulated pneumococcic pyopneumothorax. Many papers concerned with the treatment of empyema in children deal solely with one technic or another, with little or no thought of the varied underlying pathologic processes or the condition of the patient. In the literature, diverse lesions are grouped under the heading of "empyema," and favored methods of treatment are described which might be suitable for some forms of suppurative pleuritis, but prove illogical and ill conceived for others. The apparently wide differences in views concerning the treatment of empyema which exist at the present time are the inevitable result. No new procedures will be advocated in the plan of treatment to be laid down, but it is hoped that the problem of the management of pleural infections in children will be clarified on the basis of an appreciation of the varied pathologic processes and on bacteriologic studies.

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This paper is in no sense a statistical one, but a tabulation of 184 consecutive cases of suppurative pleuritis in children who came under observation at the Mount Sinai Hospital in the past few years is desirable for purposes of classification. Only those cases in which the bacteriologic studies were complete are included. The cases were collected from all four surgical services of the hospital, and the patients were treated in a variety of ways; the results can therefore be said to represent a fair cross-section of the results of treatment of empyema in children at the present time. In a future communication we shall present the results from our own surgical service, based on the principles that will be presently stated.

An analysis of the material led us to conclude that children suffering from pleural infections may be classified into well defined clinical groups, which are found to follow closely the pathologic process and the type of bacterial invasion:

1. Pneumococcus pleuritis, 56 cases, mortality, 3.5 per cent
   a. Pyothorax, 42 cases, 2 deaths
   b. Pyopneumothorax, 14 cases, no deaths
2. Staphylococcus aureus pleuritis, 45 cases, mortality, 27.5 per cent
   a. Pyothorax, 25 cases, 4 deaths
   b. Pyopneumothorax, 20 cases, 6 deaths

2 A. Staphylococcus albus pleuritis, 6 cases, no mortality
   a. Pyothorax, 2 cases, no deaths
   b. Pyopneumothorax, 4 cases, no deaths

3. Hemolytic streptococcus pleuritis, 41 cases, mortality, 18.7 per cent
   a. Pyothorax, 32 cases, 6 deaths
   b. Pyopneumothorax, 9 cases, 3 deaths

3 A. Streptococcus viridans pleuritis, 7 cases, mortality, 14 per cent
   a. Pyothorax, 6 cases, no deaths
   b. Pyopneumothorax, 1 case, 1 death

4. Anaerobic (putrid) pleuritis, 17 cases, mortality, 29.4 per cent
   a. Pyothorax, 6 cases, 3 deaths
   b. Pyopneumothorax, 11 cases, 2 deaths
5. Pleuritis with mixed bacteriologic findings, 10 cases, 2 deaths, mortality, 20 per cent

From this tabulation, it is clear that precision in diagnosis is essential for prognosis if for no other reason, and we hope to show that the plan of treatment depends on the group into which the given case of empyema falls. An accurate diagnosis can and should be made by (1) the history, (2) the physical examination, (3) roentgenograms and (4) exploratory puncture. The determination of the existence and the nature of the infection should be made in the great majority of cases by the first three procedures, and exploratory puncture should be classed as a confirmatory rather than a routine diagnostic measure. The four procedures stated are given in their order of importance.

HISTORY

The value of eliciting an accurate history cannot be overemphasized. We have frequently found that a carefully obtained story of a case has been tantamount to establishing the diagnosis. When the question of empyema is approached with the purpose of qualifying the term by its etiology, the histories tend to fall into definite groups.

Most of the cases of pneumococcus pleural infections that result in a pyothorax occur after a pneumonia. In our tabulated series thirty-seven cases were postpneumonic and only five synpneumonic. The familiar story is that of pneumonia with its characteristic symptoms of cough, sputum and fever. The temperature subsides, usually within a week or ten days, either by crisis or by lysis, and some time later there occurs a recrudescence of fever. The child has usually not been acutely ill following pneumonia, and the most prominent symptom is the persisting fever.

Pneumococcus pyopneumothorax occurs less frequently during the course of, than after a pneumonia (5:9 in our group). We wish, however, to stress the history of the synpneumonic type because prompt diagnosis, often possible from the history alone, is usually essential if life is to be saved. The onset of synpneumonic pyopneumothorax, when the cortical pneumococcus suppurative focus has ruptured into the free pleural cavity, is alarming. The history is that of a pneumonia of a severe grade, during the course of which there is a sudden onset of violent dyspnea, cyanosis, restlessness and hacking cough. With the incessant cough, more and more air is forced into the pleural cavity from the ruptured pulmonary abscess, and the symptoms are rapidly progressive. All the cases that we have seen have presented this dramatic clinical history, and the nature of the lesion was therefore realized from the history alone in recent cases. By contrast, the history of postpneumonic pyopneumothorax is not appreciably different from that of the insidious history of a simple pyothorax. Four of the nine cases in the series were encapsulated.

Since staphylococcus pleuritis is always an extension from a metastatic suppurative pulmonary lesion, the history of an antecedent infection can usually be obtained. In our series such conditions as paronychia, furuncle of the external auditory canal, staphylococcus otitis media, furuncle of the nose, umbilical infection and subcutaneous abscess were the primary sources of infection. The original lesion may have existed a week or more before the appearance of the pulmonary symptoms, and may have been so insignificant as to have been almost unnoted or forgotten by parent or nurse. The history of the pulmonary infection is that of fever and of an irritative, nonproductive cough. In some cases there were chilly sensations or true chills. Hemoptysis occurred in three instances. The toxemia results in apathy, progressive loss of appetite

and occasionally intractable diarrhea. In the histories obtained from physicians in attendance during the pulmonary condition, there were non-characteristic physical signs of pulmonary infiltration, soon followed by rapidly increasing signs of fluid in the chest.

In a few cases, the history of the Staphylococcus aureus infection was that of a pneumonitis, behaving like the usual pneumonia even with a critical drop in temperature. Although the staphylococcus was responsible for only 35 per cent of the cases in our series, a much higher proportion of the cases of pyopneumothorax in infants and very young children is caused by this organism.

The history of streptococcus pleuritis differs chiefly from the pneumococcic type in the greater severity of the course of the "pneumonia" and in the greater liklihood of the empyema being synpneumonic. Severe "pleural" pain is a frequent early complaint. Of forty-one cases the pleural infection appeared to be synpneumonic in twenty-three and postpneumonic in eighteen. All the cases of empyema that occurred after infectious diseases (measles, scarlet fever) in this series were streptococcic infections. The fluid accumulates so rapidly that it gives rise very early in the course of the illness to symptoms of respiratory embarrassment, i. e., dyspnea, cyanosis and collapse. The patients also suffer from absorption of the very toxic products, and the temperature curve is usually higher and of a more septic type than in the pneumococcic infections. There were six instances in which the underlying pulmonary lesion was possibly metastatic; once following a septic sore throat, once after an infection of the hand, once after a streptococcic peritonitis and in three cases after an acute mastoiditis. There was a case of traumatic hemothorax secondarily infected by the streptococcus.

In spite of the fact that putrid empyema occurred in 10 per cent of the cases in our series, the group is not well known in children. The lesion is usually the result of the rupture of a putrid (anaerobic) abscess of the lung. Of the seventeen cases, twelve followed the rupture of a chronic pulmonary abscess and six that of an acute abscess. A history of the underlying pulmonary lesion is easily available. The first symptoms of anaerobic pulmonary suppuration appeared within two weeks after an operation (tonsillectomy in thirteen cases) or after the aspiration of a foreign body. We have, however, seen occasional instances, not in this series, in which the etiology was unknown. Fever, foul expectoration, chills, occasionally hemoptysis and especially the fetid odor of the breath in the absence of fetid sputum characterize the history of this condition. Pain in the chest is an important symptom, and we have found in a large group of cases not in this series that the site of the initial pain is an important point in the localization of the pulmonary focus. The invasion of the pleural space is usually by direct rupture of the pulmonary abscess, although putrid pleural infection may

occasionally result from seepage from a subpleurally placed pulmonary focus. Putrid empyema, therefore, usually begins with acute and often alarming symptoms. The child becomes extremely toxic, dyspneic and markedly cyanotic. Rupture may occur within a few days of, or years after, the onset of the pulmonary symptoms. An acute, diffuse anaerobic infection of the lung (three cases) gives rise to an extensive putrid gangrenous pneumonia, frequently with multiple ruptures into the pleural cavity. The history of these cases is of short duration and is that of an overwhelming infection to which the patient rapidly succumbs.

PHYSICAL EXAMINATION

Physical examination is the most important factor in determining the type of treatment to be instituted. Only a few features will be referred to in this paper. Close attention should be given to the general examination, even when an empyema is obvious. There are instances, for example, in which the pleural infection is part of a septicemia and perhaps only an incidental part, and a properly conducted general examination can establish this fact. Frequent careful general surveys of the patient may be rewarded by revealing other suppurative foci even after the empyema has been cared for. Indeed, the general physical examination may be of vital importance after operation for empyema when the patient is not doing well and the evidence points to adequate drainage of the pleural lesion.

Even in the absence of any etiology for a putrid abscess of the lung, a foul odor of the breath on coughing is almost always pathognomonic of that lesion. Early clubbing of the fingers is common in putrid pulmonary abscess. These two signs, associated with the evidence of a pleural infection, establish the existence of a ruptured putrid abscess of the lung.

The customary physical signs of fluid in the pleural space require no extended discussion. Flatness on light percussion is by far the most significant one in our opinion. Similarly, light percussion may demonstrate the presence of tympany (and therefore of a ruptured abscess of the lung) even in the absence of any auscultatory signs of pyopneumothorax. Inspection of the chest will often furnish valuable data. In addition to the commonly observed limited expansion of the affected side, the intercostal spaces often bulge with large amounts of fluid. This evidence, together with a visibly displaced apical impulse, dyspnea and cyanosis, establishes the existence of a mobile mediastinum and the imperative necessity for closed drainage if surgical therapy is urgently indicated. Localized tenderness on pressure and circumscribed increased local heat are sometimes of real value in the diagnosis and localization of a sacculated empyema, especially after a collection of pus has been evacuated and an additional empyema is suspected.

ROENTGENOGRAPHIC ASPECTS

It is not within the scope of this paper to discuss in detail the roentgenographic aspects of diagnosis. We wish, however, to point out certain features that not infrequently offer difficulties. A basic reason for error in the interpretation of shadows in the flat film is the frequent failure to visualize the chest in three dimensions. A film of the chest taken with the child in the supine or prone position may be negative because the fluid is dispersed in a thin layer over the entire surface of the lung and is therefore of insufficient density to cast a shadow. There is, in addition, so much distortion in films taken with the child lying down, that a roentgen examination may as well be omitted if a film with the patient in the erect position cannot be obtained. In a number of our postoperative cases the films indicate that the chest was free from fluid when the child was in a recumbent position, and a large collection with a fluid level was apparent when the picture was taken with the child in the erect position. Another discrepancy for which we can offer no explanation is a negative film, even though properly taken, in a proved case of empyema. We have seen several instances in which the films taken shortly before operation were negative and in which a frank empyema was encountered at operation. The differentiation of pleural thickening from pleural effusion is often difficult in x-ray films, especially when fluid is not present in large amounts. Pleural thickening is to be suspected when the medial border of the shadow presents a more or less straight line, whereas the shadows cast by most diffuse (not encapsulated) pleural effusions present a concave border. It is not infrequently impossible to determine from x-ray films which condition is present in doubtful cases, and far greater reliance should therefore be placed on the clinical aspects. This statement holds true particularly after drainage of an empyema, when retention of pus in the region of the operative field is suspected.

We have made a number of errors in the roentgenographic differentiation between localized pyopneumothorax and abscess of the lung. An unusually large collection of air and fluid is much more apt to be in the pleura than in the lung. The presence of air above a fluid level, shifting freely with changes of posture under fluoroscopic observation, is fairly characteristic of pyopneumothorax. This phenomenon, however, may not be observed if the pyopneumothorax is more or less widely surrounded by lung. In fact, pyopneumothorax and large abscesses of the lung are indistinguishable roentgenographically in not a few instances. Even at operation the precise nature of the lesion may not be recognized, and therefore the better the operative exposure the more apt is the correct interpretation to be made.

The shadow cast by an effusion located behind the heart may be completely obscured by the cardiac shadow in the anteroposterior film.

When a retrocardiac shadow is suspected, films must be taken in the exact lateral position, in order to bring out the normally clear retrocardiac area. In fact, lateral films may be of great value in the precise localization of many encapsulated pleural effusions.

Mediastinal empyema is to be strongly suspected from the x-ray film when the heart and mediastinum are markedly displaced and the pulmonary fields are clear. The lesion may require roentgenographic differentiation from congenital disease of the heart and from pericarditis with effusion. Enlargement due to congenital disease of the heart may be ruled out if the shadow extends upward from the cardiac shadow over the root of the great vessels. The picture likewise is not produced by pericarditis with effusion, unless the effusion is tremendous. The presence of visible pulsation in a shadow seen by fluoroscopy does not negate the diagnosis of a mediastinal empyema because transmitted cardiac pulsation is always present. At times the heart and mediastinal empyema cast a single shadow in which there may be a difference in density on either side of the cardiac area.

The clue to the diagnosis of supradiaphragmatic empyema is the presence of well defined physical signs of fluid (especially on percussion) in the lower part of the chest, with an x-ray film more suggestive of pneumonitis than of fluid. A subphrenic abscess can give rise to an x-ray picture identical with that of a supradiaphragmatic empyema. Since aspiration may fail to reveal pus in mesially placed supradiaphragmatic empyemas, pneumoperitoneum may have to be resorted to for a contrast picture or for the differentiation from subphrenic abscess.

An interlobar effusion (empyema) is rather frequently reported from the x-ray film, and yet that lesion is most unusually encountered at operation in our experience. Indeed, we have come to the conclusion that an interlobar empyema is the result of a ruptured pulmonary abscess that has broken into the interlobar space, and that the interlobar surfaces of the lungs are very exceptionally the sites of abscesses. Of course, encapsulated empyemas can be situated in the neighborhood of the interlobar fissure as well as anywhere else in the pleura, but that is not what is meant by interlobar empyema. There is a characteristic film of interlobar empyema that is but rarely seen, and the roentgen diagnosis of the condition should rarely be made. The reason for stressing this point is that the operative treatment of interlobar empyema may be difficult and inevitably involves opening the free pleural cavity, while the drainage of an encapsulated empyema (whether situated at the interlobar fissure or elsewhere) should usually be a simple procedure without entry of the uninvolved pleura.

Enough has been stated to indicate the pitfalls that may be encountered if too great reliance is placed on the roentgen diagnosis of

empyema. The x-ray film and fluoroscopy are of unquestionable and sometimes of decisive aid, but should be considered in correlation with clinical data and not as independent diagnostic measures.

DIAGNOSTIC ASPIRATION

This is performed in practically all cases of suspected empyema. Much has been written concerning sudden collapse or death following exploratory puncture, but little has been mentioned concerning other aspects of the procedure. We wish to stress here the statement made at the outset, that pleural puncture should be considered a confirmatory procedure. The diagnosis of empyema should be fairly well established in the great majority of cases before aspiration is performed. Indeed, the puncture should not be considered so much a diagnostic procedure as a determination of the nature of the fluid. Viewed in this light, the procedure should be properly considered an essential step in the therapeutic indication.

In the absence of adequate evidence of pleural fluid, exploratory aspiration is never warranted. A negative puncture may result in injury to the lung, with hemoptysis or hemorrhage into the pleural space. The latter is prone to infection, especially in the presence of an active inflammation of the underlying lung, so that an empyema may develop that was not present at the time of aspiration.

Many empyemas are encapsulated, and considerable thought should be given to their approach by the aspirating needle. Selection of the standard seventh or eighth intercostal spaces posteriorly may prove unwise if the encapsulation is not nearest the surface in that area. A negative aspiration in the presence of an empyema is just as disconcerting as a positive aspiration through uninvolved pleura with resultant leakage of pus into a clean field. Not a few so-called secondary empyemas are the result of the entrance of pus into an uncontaminated part of the pleural space either by aspiration or at the time of operation. Except in unusual cases, pus should be obtained by superficial aspiration of the pleural space if the correct site has been selected. A deeply situated empyema is not proved to exist merely because pus is encountered by deep aspiration, for overlying lung may have been traversed to reach a peripheral part of the collection of pus. Accordingly, such a point should not ordinarily prove to be the site of election for the operative approach.

The physical signs and the x-ray film are the guides to the site for aspiration. Aspiration should be done at the point of maximal flatness on percussion and at the site at which the film suggests that the fluid is nearest the surface. The effort should be made to visualize the film in three dimensions and not as a flat surface. The shoulder girdles and the mass of the pectoral muscles lie on the chest, but are for the most

part off the upper thoracic cage. Although there appear to be some areas of predilection for encapsulated empyemas, sacculated effusions may occur anywhere in the pleural space, and the smaller and more mesially situated ones call for the greatest care in localization and in the approach by the aspirating needle. We have, for example, found it necessary to aspirate above the clavicle for a supra-apical empyema, or just lateral to the transverse process of a vertebra for an empyema on the mediastinal aspect of the pleura.

In putrid empyema the disclosure of foul pus by aspiration must be followed promptly by operation. Furthermore, the tract of the aspirating needle must be split open at the time of operation. We cannot stress too strongly the danger of delay in operating when aspiration has revealed foul pus. A rapidly spreading, virulent, putrid phlegmon of the chest wall is apt to be the result, and we have seen at least six deaths from this cause. Another feature of the putrid empyema that should be mentioned is the elevation of the diaphragm that results when the pulmonary abscess (the cause of the putrid pleural infection) has been of long standing. A low exploratory aspiration may readily traverse the diaphragm, and in one case in this series actually resulted in a putrid subphrenic infection.

TREATMENT

From what has already been stated, it is evident that no routine operative method can be employed in the treatment of the varied pleural infections that are included under the term "empyema." In fact, no rational therapy is possible without the recognition of the specific pathologic process in a given case. We view Potain aspiration and its modifications as illogical and dangerous, even as temporary measures, although we are aware of the fact that some patients have made permanent recoveries without any additional treatment. This view was arrived at after mature consideration. In the first place, the relief that is obtained is usually minimal and transient. Secondly, the procedure is apt to be painful, is ill suited to children, and may result in "pleural shock" or puncture of the lung. Thirdly, the withdrawal of infected fluid by suction invites greater inflammatory reaction in the wall of any inflamed cavity. In the fourth place, the desired tendency toward fixation of the mediastinum and the underlying lung is disturbed each time that the purulent fluid is withdrawn. Like other observers, we have repeatedly noted temporary relief of dyspnea and cyanosis and some approximation of the apical impulse to its normal position, only to see the return of the symptoms and the recurrence of shift of the apical impulse within the space of a few hours. Fifthly, repeated Potain aspirations are exhausting to the patient, and they are entirely ineffectual in withdrawing thick pus. Finally, adhesions that tend to convert a

unilocular empyema into one of the multilocular type are invited by the procedure if frequently repeated, and we have seen several instances in which the operative treatment has been rendered more difficult and of necessity much more extensive.

What then shall be done for a child suffering from a seropurulent pleural effusion with great mechanical respiratory and circulatory embarrassment, and toxic absorption as well? If the pleural infection is pneumococcic, the probability is that this phase will be of short duration. On the other hand, patients suffering from staphylococcic and, more particularly, streptococcic pleural infections may require relief while the fluid is still thin and the mediastinum mobile. Open drainage is obviously contraindicated. We employ closed drainage in all such cases, not only as a measure of temporary relief, but also because it may prove to be the sole operative treatment required to effect a cure. The arguments against premature drainage of empyema—inflammation still present in the lung, collapse of the lung following the entry of air into the pleural cavity and embarrassment of the function of the opposite lung—fall to the ground if a safe and properly performed method of closed drainage is utilized.

Many varieties of closed drainage have been advocated. The one that we employ is simple and safe, and can be carried out without removing the child from bed. Local anesthesia usually suffices. After aspiration has revealed pus, the needle is left in situ. A short incision is made through the skin, the needle being freed down to the intercostal musculature. A tube of suitable bore, with several lateral holes near its tip and with a clamp shutting off the other end is employed for drainage. The tip is grasped with a dressing forceps (or clamp) and plunged through the intercostal muscles into the pleural cavity alongside the needle. The latter is held steady with the free hand during the maneuver, and is withdrawn as the tube is inserted. The introducer is then removed. The distal end of the tube is now connected with a long piece of tubing placed and weighted under water in a pail on the floor (or at an appreciably lower level than the chest). The end of the long coil of tubing should be at the bottom of the pail. The clamp is removed to permit the pus to escape into the water. The tube, fitting snugly into the empyema cavity, is fastened to the skin of the chest wall with strips of adhesive. When the introduction of the tube has been properly performed, the system remains air-tight for from five to seven or eight days. By this time, leakage alongside the tube is no longer dangerous.

Although this crude method of establishing closed drainage has proved satisfactory in many cases, we have recently improved on it in two respects. A calibrated rubber tube has been devised,[1] so that the

1. Touroff, A. S. W.: Ann. Surg. **94**:955 (Nov.) 1931.

length of tubing within the pleural cavity is known. The blunt introduction of a tube through the chest wall is a procedure accompanied by considerable trauma, and therefore a special sharp-pointed bivalve introducer has been devised [2] for this purpose. These two modifications have made for precision and celerity in what should always be a simple, minor procedure. A calibrated glass receptacle at the side of the bed into which the pus drains under water makes possible the daily measurement of the amount of discharge and renders easier the study of the progress of the case. The tubing should always be of sufficient length so that no change in the position of the child will draw the far end of the tube out of the water. The clamp or weight attached to the tube at the bottom of the receptable should not be too heavy, lest the tube be withdrawn from the chest by some unexpected shifting of the child.

The time for the discontinuance of closed drainage or for a change from closed to formal open drainage depends on many factors, and a fixed rule in this regard can obviously not be laid down. Drainage through the closed system may stop within a few days. This is rarely due to the clearing up of the pleural infection. It is much more apt to be ascribable to an obstruction to drainage or to the presence of pus that is too thick to escape through the tube. Suction by means of a hypodermic syringe, the needle of which is plunged into the lumen of the drainage tube proximal to a point at which the tube is pinched, may start the flow of pus. A negative pressure so great that the plunger forcibly recoils on release indicates a plugging of the tube. Gentle continuous suction by the two-bottle method or one of its modifications may be tried, but we have found that suction is rarely indicated. If drainage stops prematurely, it is better to change the tube, at the same time taking every precaution to avoid the entrance of air during the change of tubing and leakage of air alongside the new tube. The latter can usually be obviated by packing gauze between the tube and the skin, but a tube of larger diameter may have to be inserted. If the amount of drainage has been inadequate, the fact that a child is afebrile and appears to be doing well after the establishment of closed drainage does not prove that the pleural infection has cleared up. Under such circumstances, the physical signs and roentgen examination will demonstrate the existence of fluid. Its evacuation is imperative despite the apparently satisfactory clinical course. In many cases subacute and chronic empyema will be avoided if this important point is borne in mind. Closed drainage should be discontinued only when the drainage has been adequate and the physical signs and roentgen examination prove that the pleural infection has subsided and the affected lung has expanded.

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2. By A. S. W. Touroff.

The change from closed to open drainage is indicated when the discharge is inadequate and the pus is sufficiently thick to lead to the assumption that the mediastinum is fixed. The open operation is rarely urgent after closed drainage has been employed because the acute, more grave symptoms have already been relieved, in part at any rate.

The discussion of closed drainage was begun in regard to seropurulent effusions in children who were too ill to await safely the formation of thick pus and the firm fixation of the mediastinum. It was suggested that this is particularly the case in the streptococcic pleural infections. But enough has been said to indicate our view that closed drainage should always be the primary operation whenever there is doubt as to the fixation of the mediastinum or as to how much shock the child will withstand. The less encapsulated or, to put it in another way, the more nearly total the empyema, the greater is the indication for closed drainage. Furthermore, the younger the child, the greater is the desirability of closed drainage. In infants recourse to closed drainage as the invariable primary operation has led to a pronounced reduction of the mortality rate.

Little need be said about the general technic of the open operation for empyema in children. Whether a shorter or longer intercostal incision should be used, or whether a portion of one or of more ribs should be excised, depends on the duration of the empyema and the extent and number of sacculations of the cavity. We usually prefer a liberal incision with partial costectomy of one rib, evacuation of the pus by suction, inspection of the interior of the cavity with a sterile light in order to determine if additional pockets exist and the insertion of drains under direct vision. Tubes are used for the larger empyemas, and iodoform gauze packings are introduced to the limits of the cavity (often with the addition of a tube) for the smaller, encapsulated lesions. We rarely employ irrigating fluids after operation, since there is usually no indication for their use if the operation has been adequately performed. Tubes are frequently changed after operation, the guide to their reduction in size or number, or their discontinuance, being the direct inspection of the wound, the clinical course, the physical signs and the roentgen examination. On the other hand, when gauze packings have been employed, they are usually left in place for about one week or until such time as they have become freely loosened by the discharge. Once they are removed, a clean granulating space is left for which repacking is usually not necessary. Problems encountered at operations for empyema will be subsequently discussed.

The most common indication for a primary open operation is a pneumococcus empyema with thick pus, in a child in good condition. Any form of empyema in which there is sharp encapsulation indicates an open operation. A ruptured subpleural suppurative focus with well

encapsulated pyopneumothorax comprises the third indication. Special reference will later be made to ruptured putrid abscesses of the lung with putrid empyema.

The problem is an entirely different one when a pneumococcic cortical abscess of the lung ruptures into the free pleural cavity. Attention has been called to the acute symptom complex that develops under such circumstances. The manifestations are particularly alarming when the accident occurs during the acute phase of a pneumonic process. Closed drainage is urgently indicated, regardless of how ill the child may be. We have seen recoveries in instances in which the prognosis appeared hopeless at the time of operation. Of prime importance are prompt recognition of the condition and equally prompt institution of closed drainage. Large quantities of air as well as pus may bubble through the water in the drainage bottle for days, to cease finally when the site of perforation is sealed over. In not a few instances, however, a localized pyopneumothorax remains. When the child's condition becomes sufficiently satisfactory to warrant a formal operation, the excision of one or more ribs is performed and the cavity is fully laid open. Not only the bronchial fistula but also all the recesses of the cavity should be visualized. Packings are inserted in the limits of the recesses. On their later removal, a clean dead space remains. The cavity becomes a cleft, which heals down to the bronchial fistula. The latter is often slow in closing, its healing depending on the formation of granulation tissue, which extends over and into the fistula from the adjoining pleural surface. In these cases we have never seen a permanent fistula requiring a plastic operation for its closure when the pyopneumothorax had been adequately laid open and the wound had been kept patent until the fistula had had a chance to heal over.

In infants the staphylococcus is by far the most common organism in pleural infections. As has been previously pointed out, the pleural invasion is derived from a metastatic subpleural furuncle in the lung. The reason for the high mortality in these cases is clear, as the pulmonopleural lesion is frequently only one of a number of metastatic suppurative foci. Even in these cases, however, careful search for, and adequate drainage of the metastatic foci as they appear may lead to recovery if vital organs are not involved. The pleural infection is always in the foreground, and is the first lesion that calls for treatment. There are two types of involvement of the pleura. Perhaps the more common is the one that results from rupture of the staphylococcic subpleural pulmonary focus, with the alarming symptoms of tension pyopneumothorax, with shift of the heart and mediastinum. The indication for immediate closed drainage is obvious. This procedure may prove not only palliative but also curative, if the ruptured focus (and its consequent bronchial fistula) is not large. Should there be a residual

pyopneumothorax after the acute phase has subsided, the operative treatment is identical with that described in the previous paragraph. The second type of staphylococcus empyema that we have seen presents no distinguishing clinical features from the ordinary synpneumonic or postpneumonic variety. Its presence can only be suspected because there had previously been a furuncle or other suppurative lesion, especially if the patient is an infant. The diagnosis of staphylococcus empyema can be definitely established by aspiration. In these cases closed drainage should be instituted. In all the cases that we have seen, this procedure was followed within a day or two by the escape of increasing quantities of air in the under-water drainage system. In other words, this second type of staphylococcus empyema is also due to a cortical abscess of the lung, but the primary pleural infection has been by seepage rather than from gross rupture. The fact that the lesion ruptures so soon after drainage has been instituted suggests that the mechanical factor of the closed drainage system may be the cause. In any event, the free escape of air under water obviates the likelihood of tension pneumothorax. The rupture of the pulmonary abscess virtually "blows out" more or less of the lesion in the lung. The lesion was completely "blown out" in all the cases that we have seen in infants. On the other hand we have found it necessary, in older children (and in adults), to seek for and drain more adequately the ruptured pulmonary focus from which the staphylococcic empyema was derived.

A ruptured putrid abscess of the lung results in a putrid empyema, which requires prompt surgical treatment. Well defined pleural adhesions are usually present at an early stage of the pulmonary process, so that open operation can and should be proceeded with as soon as the diagnosis has been made. The foul empyema should be widely opened by liberal excision of a rib, and the full limits of the cavity visualized. Small additional adjoining loculations are often present, and operation should not be discontinued until these are adequately laid open. They generally follow the line of the rib that was removed at the beginning of the operation, so that more and more of the rib may have to be excised in order to open up freely all of the foci. The principles that are involved in the treatment of putrid empyema are not only adequate drainage, but also wide unroofing for the free entry of air. A small opening with a drainage tube in place is entirely inadequate in the treatment of an anaerobic empyema. On the other hand, the incredibly rapid disappearance of a putrid, gangrenous pleural infection following an operation that adequately unlocks the pocket or pockets is one of the most dramatic incidents in the surgery of suppuration. A profoundly toxic state often gives way to convalescence within twenty-four hours. Not only has the empyema been properly treated, but the ruptured putrid abscess of the lung may be cured at the same time, particularly if the abscess is acute.

The reason for this lies in the fact that the lung abscess is situated subpleurally in all cases, and in rupturing, its roof is widely opened. A bronchial fistula is invariably present, and entrance of air into the interior of the pulmonary abscess cavity is both by way of the bronchial tree and, from the outside, by way of the opened pleura.

At the close of the operation for putrid empyema, all deep recesses should be loosely packed with iodoform gauze and tubes inserted, chiefly to maintain a widely open wound. Oxygen or air can be bubbled through the tubes into the empyema cavity after operation, but artificial ventilation is rarely needed to overcome the putrid infection. Every precaution should be taken to prevent the wound from closing until the anaerobic infection has completely disappeared and the bronchial fistula or fistulas are healing. In cases of ruptured chronic abscess of the lung a persisting bronchial fistula is desirable if the anaerobic infection of the lung has been only partly relieved by rupture. In our experience there has been no indication for the surgical closure of a bronchial fistula when the abscess had previously ruptured. Our difficulty rather has been to maintain its patency for a period sufficiently long for the anaerobic infection to have disappeared as a result of prolonged ventilation.

GENERAL PROBLEMS ENCOUNTERED AT OPERATION

Of the general problems to be considered, the first is concerned with diagnostic aspiration. Pus may have been readily obtained on preliminary diagnostic puncture and yet cannot be later withdrawn by aspiration at the same site when the patient is on the operating table. The position of the child on the operating table as well as the shift of the scapula when the patient is placed in position for operation must both be considered. Aspiration should be repeated with the child sitting up. It may be necessary to review the physical signs as well as the roentgen observations, and it is essential that the x-ray film be on view in the operating room. Indiscriminate punctures as regards their number and location are evidences of panic on the part of the surgeon, and at best can disclose the empyema only by sheer accident. It is unwarranted to proceed with operation in the face of negative puncture on the operating table merely because pus had previously been obtained on aspiration. The free uninvolved pleura will probably be entered if the surgeon is rash enough to assume that he will readily encounter a large collection of pus. One need only mention the complications that will in all probability result from the contamination of the normal pleural space by pus spilled from a localized purulent collection. Little pus may have been present at the exploratory puncture before operation and the child may recover spontaneously. In other instances the pus may have been derived from inadvertent aspiration of an abscess in the underlying lung and not from the pleural space.

Another problem is the procedure indicated when cloudy fluid is obtained on aspiration at the operating table when frank pus had been withdrawn in the same region before operation. Repeated aspirations may reveal nothing more in those instances in which the empyema is small, situated in a recess and found only before operation by a fortunate accident which cannot be repeated. Since the cloudy fluid represents the result of pleural reaction in the immediate region surrounding the collection of pus, the empyema can be safely approached through that portion of the pleura in which the cloudy fluid is lodged. After the thoracic incision and evacuation of the cloudy fluid by suction, the cavity is inspected by means of a sterile light introduced into its depths. A fibrinopurulent septum will then be seen shutting off the true empyema. The latter can be evacuated into the space that was previously occupied by the contaminated cloudy fluid, or a portion of an additional rib may be excised and the collection of frank pus directly drained.

A serious situation exists when the free pleura is opened during the drainage of an encapsulated empyema. This accident may be obviated in most instances if the excision of the rib at the beginning of operation is limited to that portion which directly overlies the actual roof of the empyema. The technic is simple and safe. After the pus has been evacuated by suction and the interior of the cavity inspected, the surgeon is in a much better position to remove safely as much rib as may be required for adequate drainage. Reliance should be placed on inspection and not on the sense of touch, since delicate walling-off adhesions may be readily torn by the exploring finger. It is not always a simple matter to deal with a pleural rent, and there are situations in which it may be best to place a packing in the gap. Usually, however, the rent can be securely closed if the lung is grasped and broadly approximated to the soft parts of the incision in the chest wall by mattress sutures. An attempt to suture the delicate pleural surfaces is apt to result only in a larger rent. For deeply situated pleural tears, depending on their location, a lappet of lung may have to be sutured to the adjacent structures, such as the diaphragm and pericardium. The opening of the free pleura in cases of putrid empyema is almost always followed by a generalized and usually fatal putrid pleural infection, regardless of whether the rent has been sutured or not. Suture of the opening and drainage of the free pleural cavity are both indicated if such an unfortunate accident occurs during the course of operation for a putrid empyema.

This paper deals primarily with empyema and not with abscess of the lung, but some reference should be made to the procedure indicated when it is found that a pulmonary abscess and not an empyema has been opened. The first essential is to close the free pleura if it has been inadvertently entered. The next step is to lay open the abscess to its full limits, splitting the overlying lid of lung radially to accomplish this

purpose. The shell of lung overlying an abscess is usually thin, relatively avascular and practically always adherent to the parietal pleura. Bleeding from the incised lid of lung is readily controlled by the introduction of packings in most instances, but if a freely bleeding vessel is seen, a hemostatic suture should be passed through the adjacent pulmonary tissue and not too tightly tied. In splitting open the roof of the abscess, great care should be taken to avoid entering the free pleura if it has not already been opened at the outset; the lesion must nevertheless be fully laid open at the primary operation. The problem differs when the free pleura has been entered, and a pulmonary abscess and not an empyema has been recognized as the source of the pus obtained by aspiration. The abscess of the lung is thus intact, except at the site of puncture. Inspection and palpation of the surface of the involved lung will establish the optimal site of drainage invariably in a region in which there are adhesions. Should this be in the operative field, the lung surrounding the area to be drained is sutured broadly to the soft parts of the wound. Operation is discontinued and the abscess is opened at a second stage. If the site for drainage is at a distance from the operative wound, the incision in the chest wall should be closed and an approach to the abscess at the proper place should be made either at that time or at a later date, depending on the urgency of treatment and the condition of the patient. In cases of putrid abscess of the lung, one can be almost certain that a virulent putrid empyema will result from any contamination of the free pleura; if this occurs, the wound as well as the free pleural cavity should be drained. Many features concerning the operative treatment of putrid abscess of the lung cannot be considered here. We desire, however, to stress the few principles that have been mentioned, and in particular, to emphasize the necessity of widely laying open all recesses and accessory pockets. The best results are obtained by adequate surgical measures at the time of primary operation. Secondary operations for the opening of additional foci are much more difficult, more hazardous, and not as satisfactory as concerns the ultimate cure of the patient. After the abscess has been laid open, iodoform gauze is packed into the main cavity and into all of the recesses. The packings are not removed until they become spontaneously loosened, a matter of several days. A clean bed, free from odor and with one or more bronchial fistulas, is then seen. Treatment by packing the wound should be continued until all recesses have filled in. There is always a temptation to allow these clean looking wounds to heal prematurely, and prompt closure is apt to occur if this is permitted. However, premature closing may prevent adequate drainage and aeration of the anaerobic areas, with recurrence of all of the symptoms of a putrid abscess of the lung.

Another problem that may arise at operation is the question of the approach to an atypically situated encapsulated empyema. Mention has previously been made of apical, supradiaphragmatic and mediastinal empyemas. Other situations, such as subscapular and high axillary, can be added. The guiding principle, regardless of the situation, should be to approach the lesion at the point at which it lies nearest the thoracic wall. So-called "standard" sites of approach should never be employed, lest in these cases the free pleura be entered. A very low rib excision with upward retraction of the diaphragmatic portion of the lower lobe may be required for the drainage of a supradiaphragmatic empyema. The scapula must be freely mobilized to evacuate an encapsulated focus in the pleura beneath it. The first rib directly adjacent to the vertebra may have to be excised to approach a posteriorly situated apical empyema. In short, the thoracic cage in relationship to the site of the encapsulation should be carefully studied before operation in every case. The type of encapsulated empyema itself should also be considered, for it is multilocular in no small proportion of the cases. Two separate incisions may be necessary for the drainage of contiguous loculi, and such separate incisions are certainly necessary in cases of dumb-bell shaped or completely separated encapsulations.

POSTOPERATIVE TREATMENT

Careful observation and judicious treatment after operation play a vital rôle, not only in assuring the eventual recovery of the patient, but also in effecting a shortened convalescence and a reduced incidence of sequelae. The least likely cause to which to ascribe an unsatisfactory postoperative course is an "underlying pneumonia," and yet this condition is all too frequently invoked. In an analysis of autopsies on children who died after operations for empyema at Mount Sinai Hospital, pneumonia proved to be an insignificant and infrequent factor in the fatal issue. The most common causes of death were undrained or incompletely drained collections of pus in the pleura and extensions of suppuration to the pericardium. The presence of tension pneumothorax was sometimes a significant contributing factor. It is difficult to prove the existence of an underlying pneumonia after an operation for empyema, even when this lesion may actually be present. Every effort should be made to discover possible undrained collections of pus if a child is not doing well after operation. The more promptly the purulent focus is drained, the better are the chances of recovery. These secondary operations almost invariably disclose much larger collections of pus than had been anticipated beforehand from the clinical course. We have previously indicated our view that physical signs (especially flatness on percussion) are more valuable than roentgen observations in

establishing the presence of residual or new collections of pus after operations for empyema. All available methods, however, should be used in puzzling cases, including the useful delineation of the empyema cavity and sinus with radiopaque fluids. The information obtained from a film in which these are outlined may prove of decisive value. There are occasional instances in which the results of all forms of examination are negative for residual purulent collections and yet the clinical picture appears to be due undoubtedly to the presence of suppuration. Should the course be progressively downhill, exploration of the wound is indicated. Under such circumstances, we have on several occasions encountered collections of pus directly beneath a rib, even though every diagnostic method employed had given negative results.

Immediately following an empyema operation, coughing is a common symptom. It is usually more distressing than serious, and can often be relieved by changing the position of the child. Should the coughing be severe, paroxysmal or continuous, however, codeine in small doses usually suffices, but occasionally morphine must be administered. A child in whom under-water drainage of a ruptured pulmonary subpleural focus is used is apt to cough incessantly after operation unless codeine is liberally given. The indication for opiates is clear, not only to avoid exhaustion, but also to slow the respiratory rate and so attempt partially to put at rest the site of rupture.

Cyanosis and dyspnea, which were present before operation in the group of cases to which reference has been made, may persist or even be more marked for a time. The oxygen tent often proves of extraordinary value, not only in alleviating these symptoms, but also in improving the general condition of a sick child. In the presence of rapid and shallow respirations, 5 per cent carbon dioxide added to the oxygen, results in slower and deeper breathing. The oxygen therapy should be continued until there is no recurrence of cyanosis on the removal of the child from the tent.

Circulatory failure, or the state that is termed "shock," may develop immediately after operation. Attention should be directed at once to the drainage system, and one should be sure that it is functioning properly. The best general treatment for the patient in collapse is the slow-drip intravenous infusion of 5 per cent dextrose solution, to which epinephrine may be added. The rate of flow should not be rapid, regardless of how alarming the child's condition appears to be. The patient should be wrapped in hot blankets, and opiates should be freely administered if he is restless or apprehensive.

A dangerous but fortunately rare complication of closed drainage is the occurrence of a closed tension or an open pneumothorax. This may occur when the wound about the tube in the chest ceases to be air-tight,

and air is sucked into the pleural cavity about the tube. Symptoms appear only if the mediastinum is mobile. Respiratory embarrassment is marked, cyanosis develops and the pulse becomes weak and thready. The sound made by the sucking of air into the narrow wound about the tube can be heard, even at a considerable distance, as soon as the dressing is removed. Wet dressings covered by rubber tissue should be applied about the tube in the attempt to reestablish an air-tight closure of the wound. Another method of rendering the wound about the tube air-tight is to use a piece of rubber dam with a very small opening which may be stretched about the periphery of the tube and applied to the surface of the skin with collodion and adhesive straps. These methods failing, the tube should be withdrawn and the opening in the chest tightly closed by strapping with adhesive tape. A tension pneumothorax can then be relieved by permitting the air to escape from the pleural cavity through an aspirating needle introduced anteriorly and connected to a length of rubber tubing which leads under water. If pus rapidly accumulates within the chest, a new incision for closed drainage may have to be made, but it is desirable, if possible, to first await fixation of the mediastinum. A sucking wound occasionally constitutes a complication after an open operation for empyema, either because adhesions that fix the mediastinum break down or because they are not present. There should be no difficulty in recognizing the condition. The wound must be tightly strapped regardless of the presence of, or the amount of pus in the cavity. If the child suffers from the results of the retention of pus, under-water drainage is instituted by inserting a snugly fitting tube into the strapped wound or through a new small incision. Daily tests determine when the strapping of the wound may be safely discontinued.

One of the most important problems in the postoperative care of children and especially infants suffering from pleural infections is concerned with feeding. Vomiting and anorexia constitute serious complications because they reduce the child's resistance to infection. If adequate nutrition cannot be maintained by methods of oral feeding, a slow continuous intravenous infusion of 5 per cent dextrose will often tide the patient over a critical period. The veins on the dorsum of the hand are useful sites for this purpose. We recently saw an infant aged 3 months in an apparently hopeless marantic state before and after closed drainage for empyema, who was sustained by intravenous infusions continued for many days. During convalescence, repeated small transfusions of blood are invaluable as supportive measures. Abdominal distention interferes with expansion of the lungs and tends to increase the patient's dyspnea. The abdomen should therefore be inspected at

every visit, and distention, which sometimes rapidly follows operation, should be treated promptly with enemas, colonic irrigations or even solution of pituitary if necessary.

Many complications that can arise after operation for the treatment of empyema have not been referred to. Enough has been written, however, to indicate that close and constant observation of a sick child is essential for the early recognition of untoward phenomena and the prompt institution of appropriate therapy. Intelligent care will be reflected in a lowered mortality. Neither the operative nor the postoperative treatment of empyema can be standardized. The basis of sound therapy in either case is an understanding of intrathoracic mechanics and of the varied pathology of pleural infections.

SORE THROAT IN CHILDREN DUE TO STREPTOCOCCUS EPIDEMICUS

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During the winter and spring of 1931, from January to May, a bacteriologic study of infections of the throat in children was made, with particular reference to hemolytic streptococci. Among these streptococci, the type characterized by large mucoid colonies and encapsulation was identified in nine of one hundred and two patients as Streptococcus epidemicus (Davis). It is our purpose to report the occurrence in children of sporadic sore throat due to S. epidemicus and to emphasize the more frequent complications in tonsillitis due to this organism than in tonsillitis due to other hemolytic streptococci.

Sporadic sore throat in adults from whom hemolytic streptococci were isolated was found to be due to S. epidemicus in approximately 10 per cent of the patients. Up to this time S. epidemicus has been identified only in connection with milk-borne epidemics of septic sore throat. Our investigations [1] have shown sore throat in its natural state to be a sporadic disease, and that under exceptional circumstances, when epidemicus causes a mastitis in the cow, the milk becomes responsible for an epidemic among the consumers.

Among our patients, children as well as adults, the factor of milk can be excluded, because practically all of the patients consumed pasteurized milk and because in each instance the patient was the only member to be affected in a family, hospital or orphan home where numerous other members drank the same milk. In milk-borne epidemics, as a rule, several members of a family become ill with sore throat. When milk is responsible, large numbers of persons contract sore throat, and in an analysis of the source it is found that all of the patients consume raw milk from the same dairy. Our patients were in scattered parts of Chicago and obtained pasteurized milk from several dairies.

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1. Pilot, Isadore, and Davis, David J.: Sporadic Septic Sore Throat, J. A. M. A. **97**:1691 (Dec. 5) 1931.

Cultures were made from one hundred and twelve children with sore throat and fever. In several whose throats were devoid of tonsils the clinical picture was often one of intense redness of the pharynx with fever. In ten of the children the typical rash of scarlet fever developed. These patients and patients with diphtheria were excluded from the group to be studied. The clinical manifestations of sore throat in children are, as is well known, extremely variable. In our series the local change varied from a mild to an intense redness, accompanied by a grayish-white or white exudation. The temperature ranged from 100 to 105 F., and the toxic state and general symptoms usually varied with the fever.

The procedure in obtaining cultures consisted in applying a sterile swab to each tonsil, or to the red pharynx in tonsillectomized persons, and placing it in a sterile test tube to be conveyed to the laboratory. As most of the patients were seen at their homes, cultures of the swabs could not be made immediately, but in most instances they were made

TABLE 1.—*Hemolytic Streptococci in One Hundred and Two Cases of Sore Throat*

	Pure Culture	Many	Few	None	Total
Streptococcus epidemicus.....	3	3	3	93	102
Other hemolytic streptococci....	10	15	25	43	93

within twelve hours, and never later than twenty-four hours, after they were taken. To bring out S. epidemicus as well as other hemolytic streptococci of the beta type, inoculations were made into melted infusion agar to which defibrinated human blood (5 per cent) and ascites fluid (20 per cent) were added. The mixture was then poured into Petri dishes.[2]

S. epidemicus was recovered in nine of one hundred and two cases (table 1). In fifty cases, other hemolytic streptococci of the beta type were identified. Among the forty-three negative for hemolytic streptococci, four yielded pure cultures of Staphylococcus aureus. Predominant numbers or pure cultures of the streptococci were obtained in six of the nine cases of S. epidemicus, and in twenty-five of the fifty other cases. Pure cultures were most often found in swabs taken during the first forty-eight hours of illness and occasionally up to the sixth day. Large or predominating numbers of the streptococci were observed not only during the first weeks but often two and three weeks after the onset of the infection. Complications were noted more often in the children in whom the streptococcus persisted than in those whose throats no longer yielded the hemolytic streptococci.

2. Pilot, Isadore; Hallman, Blake, and Davis, D. J.: A Culture Medium for the Isolation of the Streptococcus Epidemicus of Epidemic Septic Sore Throat, J. A. M. A. **95**:265 (July 26) 1930.

The youngest person affected was 19 months of age (table 2). Older children of all ages were observed, and experience with different age groups showed that the susceptibility to sore throat extends to 50 years of age. Cultures of S. epidemicus have been obtained from the exudates of fatal meningitis or peritonitis in infants 6 months of age.

Clinically it would be difficult to differentiate sporadic sore throat due to S. epidemicus from that due to other hemolytic streptococci. During milk-borne epidemics of sore throat typical cases of a very septic type are characterized by intense, red, edematous tonsils, uvula and palate and by high fever and severe prostration. Such manifestations

TABLE 2.—*Sore Throat Due to Streptococcus Epidemicus—January to May, 1931*

Name	Age	Sex	Throat Manifestations	First Observation	Temperature	Course	Complications
R. G.	9	Male	Tonsils out, intense red throat	4th day	103	4 days	None
R. R.	5	Male	Follicular tonsillitis	7th day	104	Few days	None
P. E.	5	Female	Large red tonsils	2d day	100-103	4 weeks	Adenitis, otitis media, glomerulonephritis
A. D.	20 mo.	Male	Large red tonsils	3d week	99-103	6 weeks	Adenitis, otitis media
D. S.	10 mo.	Female	Large red tonsils	7th day	104	4 weeks	Otitis media, adenitis
C. F.	6	Female	Exudate on large red tonsils	4th day	100-104	6 weeks	Otitis media, mastoiditis, adenitis
M. F.	5	Female	Follicular tonsillitis	2d day	103	1 week	Slight cervical adenitis
W. A.	2	Male	Tonsillitis	3d week	100	6 weeks	Adenitis, otitis media
S. B.	12	Female	Exudate on tonsils	4th day	103	1 week	None

in sporadic form appear to be exceptional. In our series of sporadic cases this severe clinical picture and such findings in the throat were lacking. The sore throat due to S. epidemicus varied from diffuse redness to tonsillitis with a heavy exudate covering the surface of the mouths of crypts and of the tonsils (table 2). The temperature varied from 100 to 104 F.; the pulse was always rapid, and the patients appeared ill and toxic during the first few days. The clinical course resulted in recovery, in the milder cases, within four to seven days. The course was prolonged by the appearance and nature of the complications and sequelae.

An outstanding feature of sore throat due to S. epidemicus is the greater tendency to otitis media, cervical adenitis and other complications. In this respect the infection is more dangerous and treacherous than the sore throat associated with ordinary hemolytic streptococci

(table 3). Among the nine cases of sore throat due to S. epidemicus, five cases of cervical adenitis developed, five of otitis media, one of mastoiditis and one of glomerulonephritis. In the fifty cases due to ordinary hemolytic streptococci, five patients had cervical adenitis, four otitis media, one peritonsillar abscess, one arthritis and one endocarditis. Of great interest was the low incidence of complications in patients in whose throat there were no hemolytic streptococci. Of forty-three such patients only one had otitis media and one cervical adenitis. All of our patients recovered.

The persistence of hemolytic streptococci in the throat is an important factor in the development of complications and sequelae. In the patients with otitis media, glomerulonephritis, and other conditions the cultures of the throat and of the exudates revealed the same S. epidemicus. Our experience with adults was similar and was particularly striking in

TABLE 3.—*Complications of Throat Infections in One Hundred and Two Patients with Particular Reference to Hemolytic Streptococci*

Organism	No. of Cases	Otitis Media	Mastoiditis	Cervical Adenitis	Nephritis	Arthritis	Endocarditis	Peritonsillar Abscess
Streptococcus epidemicus	9	5	1	5	1	0	0	0
Other hemolytic streptococci	50	4	0	5	0	1	1	1
Cases with no hemolytic streptococci	43	1	0	1	0	0	0	0

patients with arthritis complicating sore throat. The arthritic manifestations coincided with the appearance and disappearance of the hemolytic streptococci from the throat. A few similar observations illustrating the importance of the hemolytic streptococci were also made on patients with complications and sequelae of erythema nodosum, empyema, sinusitis and suppurative cervical adenitis.[1]

The conditions followed sore throat due to S. epidemicus, which could be demonstrated at the time of the development of these complications. It would appear from these bacteriologic observations that S. epidemicus was not only the cause of the original sore throat, but was directly responsible for the development of the complicating lesions.

Three cultures of hemolytic streptococci were obtained from children succumbing to peritonitis at the Michael Reese Hospital. These streptococci in their cultural characteristics resembled S. epidemicus. The clinical picture in these patients was that of so-called primary peritonitis. Wile and Saphir [3] believe that the streptococci come from the throat

3. Wile, S. A., and Saphir, O.: Migratory Peritonitis, Am. J. Dis. Child. **43**:610 (March) 1932.

and that, instead of taking a hematogenous route, they cause a mild enteritis and wander through the intestinal wall to the peritoneum. In one instance the same S. epidemicus was demonstrated in the contents of the bowel and in the peritoneal exudate.

Another noteworthy complication is that of streptococcus meningitis of otitic origin. All of four strains obtained from the Cook County Hospital grew as S. epidemicus. It would appear that this streptococcus has more aggressive properties than ordinary hemolytic streptococci. These properties are probably dependent on the mucoid character of colonies and of capsules, both of which have been identified in various mucoid organisms as smooth or dissociates which have greater virulence than the rough or ordinary forms. Whether or not S. epidemicus represents such a smooth dissociate of ordinary hemolytic streptococci remains to be determined.

SUMMARY

1. Nine of one hundred and two children with sore throat yielded S. epidemicus; fifty others yielded ordinary hemolytic streptococci.

2. The sore throat due to S. epidemicus was sporadic and not related to the supply of milk.

3. The clinical picture of the patients with tonsillitis due to S. epidemicus was similar at the onset to that of the patients with ordinary hemolytic streptococcus infections, but complications and sequelae were more common in the former.

4. The greater frequency of complications may be due to the capsules and the mucoid character of S. epidemicus, properties that have been associated with added virulence and aggressiveness.

ANTITOXIN CONTENT OF THE BLOOD SERUM OF CHILDREN WITH NEGATIVE REACTIONS TO THE SCHICK TEST

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Prior to 1912, all the methods available for determining the presence of diphtheria antitoxin in the human blood involved the use of inoculations into guinea-pigs. In that year Schick [1] published the results of his studies on a test with which it was possible to demonstrate the specific antitoxin in the blood and tissues by the simple means of an intracutaneous injection of diphtheria toxin. With this method, now so well known as the Schick test, it became possible to divide human beings into two great classes from the point of view of immunity to diphtheria: (1) those with negative reactions to the Schick test whose blood contained an antitoxin titer of 1/30 unit or more per cubic centimeter of serum and who were immune to clinical diphtheria, and (2) those with positive reactions to the Schick test whose blood contained an insufficient amount of antitoxin and who were liable to have diphtheria.[2] It was determined by Schick that the amount of toxin that is completely neutralized when there is present at least 1/30 unit of antitoxin in the blood serum is 1/50 minimum lethal dose. This amount was adopted as the standard dose for the Schick test.

Because of their obvious importance, the statements cited have been the subjects of repeated studies. Glenny, O'Brien and Dudley in England, Park in America and Ramon in France have been particularly prominent in this field. All these studies corroborated the original experiments of Schick and his co-workers. Their results are conclusive and are fortified by the accumulating evidence of clinical experience pointing to the reliability of the Schick test as an indicator of a definite and significant level of immunity to diphtheria. Despite this, certain investigators, such as Kellogg and Flood in America, have reached conclusions totally at variance with those just stated. Indeed,

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1. Michiels, J., and Schick, B.: Die Intracutanreaktion des Menschen auf Diphtherietoxininjection, Ztschr. f. Kinderh. **5**:255 and 349, 1912.

2. We shall not discuss the pseudoreaction in this paper.

on the basis of studies on the Schick test and the blood antitoxin, Flood [3] has recently stated that "a negative (Schick) reaction is usually misleading."

To test the validity of this and similar statements, we determined the antitoxic titer of the blood serum of a group of children with negative reactions to the Schick test.

METHOD

The method we used is minutely described and discussed by Schick, von Groer and Kassowitz in Abderhalden's "Handbuch der biologischen Arbeitsmethoden." [4] Briefly, our procedure was as follows:

Blood was drawn from the median basilic vein of children who had reacted negatively to the Schick test performed as a routine on all patients admitted to the pediatric wards of the hospital. After obtaining the blood, the children were retested with 0.1 cc. of a 1:750 dilution (equivalent to 1/50 minimum lethal dose) of the toxin used for our antitoxin determinations in guinea-pigs.

The blood was immediately centrifugated, and the supernatant serum diluted to the proportions of 1:5, 1:10, 1:37, 1:50, 1:100 and 1:200 in a special buffer solution prepared by the Department of Health Laboratories.[5] One-half cubic centimeter of the 1:750 dilution of toxin was added to an equal amount of each of the serum dilutions. These were well mixed and placed in an incubator for two hours and then in an icebox for twenty-two hours. The toxin-serum mixtures were now ready for use, and 0.2 cc. of each mixture was injected intracutaneously into a guinea-pig. The technic of the injections was identical with that used for the Schick test in human beings.

In case of a positive reaction, one observes, after from twenty-four to forty-eight hours, at the site of the injection an area of redness and infiltration, which after from seventy-two to ninety-six hours progresses to necrosis, the intensity of the reaction depending on the amount of free toxin present in the mixture. Since the minimum lethal dose of our toxin was 0.008 cc., and since 1 unit of antitoxin is calculated to neutralize 100 lethal doses of toxin, the amount of antitoxin in each sample of serum could be mathematically determined.

COMMENT

Of the total fifty-two serums that were tested, fifty-one were obtained from children with definitely negative reactions to the Schick test, i. e., from those who had reacted negatively both to the dilution used in the ward and to our own dilution of the toxin. In only three instances were the antitoxin titers below the expected 1/30 unit per cubic centi-

3. Flood, R. G.: Blood Diphtheria Antitoxin Studies, Am. J. Dis. Child. **39:** 107 (Jan.) 1930.

4. Schick, von Groer and Kassowitz, in Abderhalden: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1924, section 13, pt. 2, no. 3, 503.

5. This solution is described by Glenny, Pope and Waddington: J. Path. & Bact. **31:**133, 1928. It keeps the toxin stable for an extended period of time.

meter of serum. The serum in one case contained less than 1/50, but more than 1/100, unit per cubic centimeter, while the serums in the two others had less than 1/30, but more than 1/50, unit per cubic centimeter of serum.

Ninety-four per cent of this series had, therefore, the minimum serum antitoxin titer originally determined by Schick. In no instance did we find an absence of antitoxin in the presence of an unquestionably negative reaction. All the serums contained varying amounts of antitoxin; forty-eight of the fifty-one had 1/30 unit or more; two showed an antitoxin content of less than 1/30, while only one child had less than 1/50 unit of antitoxin per cubic centimeter of serum.

One serum did have a titer lower than this minimum figure. This specimen was obtained from a child who was considered to have a negative reaction to the routine Schick test, given on admission, but who reacted positively to our toxin. The accuracy of our test was demonstrated by our finding less than 1/100 unit of antitoxin per cubic centimeter of serum. Since we did not test the serum for lesser amounts, it is possible that this child may have had no antitoxin in his blood. Obviously the fault lay with the toxin used in the ward, which had deteriorated and had lost the ability to cause a specific reaction. Except for the retest, this patient might have been regarded as an example of a child with a negative reaction to the Schick test, having little or no antitoxin in the blood.

Such cases have indeed been reported in the literature. Thus, Kellogg [6] stated "that more than 20 per cent of those who were Schick-negative following toxin-antitoxin immunization were Kellogg-positive, that is, they either had no antitoxin in the blood or the amount present was too small to account for a negative Schick reaction." He was inclined to blame these discrepancies on the previous injections of toxin-antitoxin, and stated that the type of immunity following this form of immunization might possibly cause a negative reaction to the Schick test with an insufficient antitoxin in the blood.

This assumption is, however, incorrect. In our series there were four children, who, according to the history, had had the three injections of toxin-antitoxin. All had demonstrable antitoxin in their blood; in no one was it below 1/30 unit (cases 10, 21, 47 and 52). The significance of these figures is increased by the fact that it is more than likely, in view of the great frequency of immunization to diphtheria in New York, that many more of our children had been rendered immune by injections of toxin-antitoxin without the intern having

6. Kellogg, W. H.: Occurrences of Schick Negative Reactions in the Absence of Free Antitoxin in the Blood Stream, Proc. Soc. Exper. Biol. & Med. **24**:141, 1926-1927.

recorded the fact on the history chart. Hence, based on Kellogg's findings, we should have encountered many discrepancies between the results of the Schick tests and the inoculations into guinea-pigs. As was stated, such was not the case.

Further evidence against Kellogg's contention may be found in the report prepared by Ramon [7] and his co-workers, summarizing their work on the immunization against diphtheria with anatoxin. Of 122 persons with positive reactions to the Schick test in whom the reaction had been rendered negative by this means, nine (or 7.37 per cent) had more than 1/30 unit per cubic centimeter of serum, and 113 (or 92.93 per cent) had more than 1/10 unit. Furthermore, 48 per cent of the total tested had more than 1 unit of antitoxin per cubic centimeter of serum.

Unquestionably, there is no difference in the degree or the type of immunity between an artificially produced negative state and one brought about by natural means (i. e., through infection). The more probable explanation of the discrepancies that Kellogg noted, namely, variations in the potency of toxin employed, will be discussed later.

These considerations lead one to regard with surprise Flood's [5] conclusion that "46.6 per cent of the children giving a negative Schick reaction did not have 1/50 unit of antitoxin." These figures are in direct contradiction to those of most observers. Thus, O'Brien [8] titrated sixty-six blood specimens by the Roemer method, and found that the results agreed with the statement that at least 1/30 unit of antitoxin per cubic centimeter of serum is necessary to prevent the Schick reaction. Similar conclusions were reached by Park [9] after a study of fifty cases.

Ramon,[7] too, categorically states: "We had, indeed, quickly convinced ourselves of the agreement between the Schick test and the presence or the absence of antitoxin." This conclusion is based on the results of 199 determinations on the blood both of persons with positive reactions and of those with negative reactions to the Schick test. Our own figures also fail to substantiate any of Flood's statements, since, as mentioned before, only one of our fifty-one children having a negative reaction to the Schick test had less than 1/50 unit per cubic centimeter of serum.

How can the marked discrepancies between the conclusions of workers like Kellogg and Flood and those of most observers be best explained? Unquestionably, the crux of the whole problem is the

7. Ramon, G., and Debré, R.: L'immunisation contre la diphthérie a l'aide de l'anatoxine, Report to the Bureau of Hygiene, League of Nations, Geneva, May 28, 1931.

8. O'Brien, R. A.; Copeman, S. M.; Eagelton, A. L., and Glenny, A. T.: Experiences with the Schick Test, Brit. J. Exper. Path. **3**:42, 1922.

9. Park, W. H.: Personal communication.

potency of the toxin employed both for Schick tests on human beings and for inoculations into guinea-pigs. The need of checking, carefully and repeatedly, the value of the diphtheria toxin has been stressed by many authors. Schick [10] has pointed out time and again that to obtain uniform results a standardized and potent toxin must be used. This is so obvious that it would seem unnecessary to mention it. Yet some have disregarded this phase of the subject, and in consequence have obtained unexpected results.

This problem was discussed at the London Conference of the Bureau of Hygiene of the League of Nations,[11] where the importance of using a standard toxin of known value for the Schick test was emphasized. Similar opinions were voiced by Jensen and by Bessau [12] at the German Pediatric Congress in 1931.

In this respect, the studies of Rhoads [13] on immunization against diphtheria are instructive. During the course of this work, he had occasion to test the potency of nine different preparations of diphtheria toxin used in the Schick test. Astonishingly enough, "Two of the commercial preparations gave practically no reaction in any of the persons tested, while the remaining seven gave positive results with varying degrees of size and brightness in the same persons." These significant results explained the occurrence of moderately severe attacks of diphtheria in two nurses who were supposedly negative to the Schick test, but who had, in all probability, been tested with an impotent toxin dilution.

Equally instructive is the work of Jensen,[14] who found that, "in 46 immunized boys only 4 (8.7 per cent) were positive to Toxin A, while 6 (12.3 per cent) were positive to Toxin B," which had a much higher combining power than the former. It is important to realize that this discrepancy in the potency of the toxins existed despite the fact that both toxins had been standardized according to the rules of the English Commission, and, accordingly, should have produced iden-

10. Schick, Béla: Diphtheria, in Pfaundler, M., and Schlossmann, A.: Handbuch der Kinderheilkunde, ed. 3 and 4, Leipzig, F. C. W. Vogel, 1931, vol. 2, p. 1. (This article summarizes Schick's views on the various problems of immunity to diphtheria.)

11. Conclusions of the London Conference of the Bureau of Hygiene, League of Nations, July, 1931.

12. Jensen and Bessau, in discussion on Schick, Béla: Active Immunization Against Diphtheria, German Pediatric Congress, Dresden, September, 1931.

13. Rhoads, P. S.: Skin Tests and Immunization Against Scarlet Fever and Diphtheria, J. A. M. A. **97**:153 (July 18) 1931.

14. Jensen, Claus: A Comparative Study of the Reactions to Schick Toxin A and B, Report to the Bureau of Hygiene, League of Nations, London, July, 1931; footnote 12.

tical reactions. That they did not do so casts no reflection on the accuracy of the English method of testing, but does illustrate the extreme lability of diphtheria toxin.

Our own experience serves to emphasize the absolute necessity of using only a toxin of unimpeachable quality. For example, as was stated, one child was considered to give a negative reaction to the Schick test after having been tested with the toxin used in the ward, but was found to have a definitely positive reaction when a toxin of proved potency was injected.

The uniformly satisfactory results obtained by workers such as Park or Ramon are of significance in the light of this discussion. Unquestionably, they are attributable to the high quality of their toxins, which are carefully standardized and repeatedly tested for potency. Park, for example, stores his toxin for a period of from one to two years, during which time the potency reaches a more or less fixed level, owing apparently to the change of part of the toxin to toxoid. Having reached this fixed state, the toxin keeps its potency for a long time and may even be diluted with special buffer solutions, as mentioned,[4] without any fear of its value being affected.

As a further check, control tests are made from time to time, and if these disclose a diminution in the potency of the toxin, the entire lot is immediately discarded. Owing to this constant and painstaking care, Park, as well as Ramon, is able to produce a toxin of uniform potency. Indeed, we attribute our high percentage of correlation between the negative Schick tests and the blood antitoxic titers to the fact that we employed the New York City Board of Health toxin and checked its potency at intervals throughout the period of our study.

There is, however, still another factor that may help to explain an occasional discrepancy between the result of a Schick test on a human being and that of inoculation into a guinea-pig. We refer to the custom of reading the test in human beings from five to seven days after the injection of the toxin, at which time, in the great majority of cases a pseudoreaction, if present, will have faded, while a true positive reaction will be easily identified as such. However, in occasional instances (and it is these that concern us now), if the site of the injection is carefully inspected at daily intervals, a slight but definite redness will be seen to appear within from twenty-four to forty-eight hours, only to disappear subsequently. When noted on the fifth or on the seventh day, the reaction is negative.

This type of reaction, discussed by Schick[15] in his original contributions, and definitely distinguishable from the pseudoreaction, is

15. Michiels, J., and Schick, B.: Die Intracutanreaktion des Menschen auf Diphtherietoxininjection, Ztschr. f. Kinderh. **5**:349, 1912.

found in persons whose serum antitoxin content is lower than 1/30 unit. In such cases there is not enough antitoxin in the blood to neutralize completely the toxin in the area into which injection was made, but it is sufficient to check the specific inflammatory reaction after an interval of from twenty-four to forty-eight hours.

Though of great importance theoretically, this transitional positive reaction has little significance clinically. Such persons will be prepared to neutralize any toxin produced at the beginning of an infection, so that, in the great majority of cases, the disease will not reach the clinical stage. Should clinical symptoms develop, the course of the illness will be benign even without specific treatment with antitoxin.

We cannot emphasize sufficiently the fact that from the practical standpoint it matters little whether a negative Schick test does or does not connote exactly 1/30 unit of antitoxin per cubic centimeter of serum in every person.[11] What is of vastly greater importance is that it permits one to separate human beings with sufficient accuracy into two broad classes, corresponding to those susceptible (having positive reactions to the Schick test) and to those immune (having negative reactions to the Schick test) to clinical diphtheria. It must be further emphasized that the term "clinical diphtheria" does not include every case of rhinitis or of pharyngitis with positive cultures. Obviously, such cases are not necessarily true instances of diphtheria. The questions of whether a person is a carrier or whether the diphtheria bacilli are virulent come to the foreground and must be answered before the reliability of a negative Schick test can be doubted.

Occasionally, a discrepancy may be found, and a person having a negative reaction may have less than the usual amount of antitoxin in the serum. But this does not speak against the value of the test. No biologic reaction gives 100 per cent results consistently. So many factors may influence the evolution of the reaction that it is not at all surprising that now and then a discrepancy does appear. Certainly, this is of rare occurrence. It is significant that Park [16] in all his wide experience has "never seen an undoubted case of diphtheria occur in a child who had recently had a negative Schick reaction after a test performed by an expert." He and his co-workers have definitely established the fact that a negative test is sufficient evidence of the ability of the individual to resist the usual type of diphtheria infection.

This statement is substantiated by the investigations of O'Brien, Okell and Parish [17] in England. They studied a series of over 20,000 persons with negative reactions to the Schick test, and found that after

16. Park, W. H.: Some Important Facts Concerning Active Immunization Against Diphtheria, Am. J. Dis. Child. **32**:709 (Nov.) 1926.

17. O'Brien, R. A.; Okell, C. C., and Parish, H. J.: "Diphtheria" in Schick-Negative Reactors, Lancet **1**:149 (Jan. 19) 1929.

a lapse of six years, eighteen had contracted diphtheria, and that in every instance except one the disease had been very mild—evidence of the ability of those affected to mobilize effectively their defensive mechanism against invasion by the diphtheria bacilli.

In the light of this discussion, statements such as that of von Mettenheim,[18] that a negative Schick reaction is "by no means synonymous with definite protection against diphtheria," are both misleading and unjustifiable. As already mentioned, absolute, consistent, test tube-like substantiation of a biologic reaction is not to be expected. Certainly, if the test indicates the correct state of immunity in so high a percentage of instances as that found by O'Brien, its reliability and usefulness are established. This is the consensus of authoritative opinion, and increasing experience further attests to the value of the Schick test as one of the most practical aids in the campaign against diphtheria.

SUMMARY AND CONCLUSIONS

1. The blood of fifty-one children with negative reactions to the Schick test was titrated for the antitoxic content.

2. Forty-eight, or 94 per cent, had at least 1/30 unit of antitoxin in each cubic centimeter of blood serum.

3. In one case the value was between 1/50 and 1/100, and in two other cases, between 1/30 and 1/50 unit per cubic centimeter of serum.

4. In no instance did we find a child with a negative reaction to the Schick test with no antitoxin in the blood.

5. Reported discrepancies, such as finding persons with negative reactions to the Schick test with little or no antitoxin in the blood, can in all probability be ascribed to the use of a toxin of questionable potency.

6. A standardized, potent toxin is essential for obtaining consistently correct results. Without such a toxin, errors will invariably creep in.

7. Occasionally, a reaction to the Schick test will be positive within from twenty-four to forty-eight hours, but will become negative thereafter. This type of reaction is found in persons having less than the usual 1/30 unit of antitoxin per cubic centimeter of serum.

8. From the point of view of immunity to diphtheria, such persons are of no practical importance, since they possess an efficient barrier against the development of clinical diphtheria.

9. Experience has proved beyond any doubt that the Schick test, correctly performed, is a practical and reliable indicator of the presence of diphtheria antitoxin in the blood in an amount sufficient to protect the individual against clinical diphtheria.

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18. von Mettenheim, H.: Schutz und Heilmittel der Diphtherie, Med. Welt **5**:1593 (Nov. 7) 1931.

TREATMENT OF EXTRAPULMONARY TUBERCULOSIS WITH METHYLATED ANTIGEN

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A few years ago it occurred to certain French observers that the preliminary removal of the fatty portion of the tubercle bacillus might facilitate the production of a more potent antigen for use in the treatment of tuberculosis. In brief, this was accomplished by extracting the killed and dried tubercle bacilli with acetone. The acetone was then removed by filtration, and the defatted organisms were suspended in methyl alcohol for some days and then filtered. The filtrate thus obtained was designated methylated antigen, and after suitable dilution with physiologic solution of sodium chloride was injected into laboratory animals and later into man.

In 1925, Negré and Boquet [1] reported the results they obtained with methylated antigen in tuberculous guinea-pigs and rabbits. They concluded from these experiments that antigen thus prepared when injected into animals was capable of provoking an abundant production of antibodies to increase their resistance to tuberculosis. Doses of 0.5 cc. for guinea-pigs and 1 cc. for rabbits given once or twice a week to infected animals definitely retarded the evolution of the disease. Treated animals outlived controls for many months, and their lesions were less numerous, more discrete and showed a tendency to fibrose. The only adverse reaction was the production of slight fever.

In 1926, these authors [2] and, in 1927 Valtis [3] reported the use of methylated antigen in human cases of extrapulmonary tuberculosis. Their plan of treatment consisted in the subcutaneous or intramuscular injection of increasing doses at decreasing intervals. They claimed that this produced fewer reactions, either focal or general, than did the injection of other types of tuberculin. Fever was rare, but a rise in temperature of a fraction of a degree might occur in hypersensitive persons. In most cases, amelioration of symptoms was noted after four or five

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1. Negré, L., and Boquet, A.: Ann. l'Inst. Pasteur **39**:101 (Feb.) 1925; Presse méd. **33**:1315 (Oct. 3) 1925.

2. Negré, L., and Boquet, A.: Presse méd. **34**:370 (March 24) 1926.

3. Valtis, J.: Progrès méd. **42**:1073 (July 9) 1927.

injections, and weight, appetite and general strength improved. More recently, Boquet and Negré [4] concluded a paper on the value of antigen in the treatment of tuberculosis with the statement that surgical tuberculosis can be cured and a remedial effect be produced in renal and in certain forms of pulmonary tuberculosis by injections of methylated antigen.

Since the fall of 1926, methylated antigen has been used at the Hospital for Sick Children in the treatment of more than sixty patients with external tuberculosis. The antigen was secured from the Pasteur Institute by one of us (H. P.). The same technic was employed as that used by Boquet and Negré. Starting with the dilute antigen, doses of increasing strength were injected once or twice a week, depending on the nature of the case. After a dose of 1 cc. of dilute antigen had been given twice, concentrated antigen was used and similar doses given. The initial dose was 0.25 cc. This was repeated once, and thereafter every second dose was increased by 0.25 of 1 cc. until 1 cc. was given, and then concentrated antigen was used in the same doses. When a dose of 1 cc. of concentrated antigen had been given twice, a course was completed and many patients were able to discontinue treatment. When further administration was deemed advisable, 1 cc. of concentrated antigen was given weekly for as long as it was desired. No larger amount was ever given at one time. A course, which is the minimal number of doses required, extends over approximately four months. This is only from a fourth to a third of the time previously required in attempting to produce similar results with *Bacillen* emulsion. A fair idea of the probable value of antigen in a particular case can be gained after the first three or four injections. So frequently do the acute symptoms subside by this time that some patients foolishly stop treatment, and subsequently suffer a relapse which necessitates starting treatment all over again. The absence of noticeable improvement by the end of four weeks makes it doubtful whether further injections are justified.

Reactions are uncommon, but they occur in a few patients with sufficient severity that treatment must be discontinued. In those with less severe reactions smaller doses with a more gradual increase in amount are indicated. A mild febrile reaction is not infrequent. Both local and focal reactions occur, the former as a reddened indurated area at the site of inoculation, the latter, which are less common, as a transitory exacerbation of the tuberculous condition. In no case was there any evidence of reactivation of a quiescent pulmonary lesion. Reactions are seen more often in glandular cases than in any others.

4. Boquet, A., and Negré, L.: Ztschr. f. Tuberk. **60**:301 (May) 1931.

The following summary of the cases in which treatment was given at the Hospital for Sick Children will give an idea of the results to be expected.

SUMMARY OF CASES

Tuberculous Cervical Adenitis (Fifteen Cases).—Courcoux [5] treated thirty patients with tuberculous adenitis with methylated antigen and reported good results in the majority. Similar results were also obtained by Bernard and Valtis. These workers stated that after four or five injections the periadenitis disappeared, and the glands became discrete and then decreased in size and were completely absorbed in three or four months. We were unable to duplicate these results. Only six of our fifteen patients were completely cured. One other was temporarily

TABLE 1.—*Tuberculous Cervical Adenitis Treated with Antigen*

Case	Age	Duration of Treatment, Weeks	Number of Doses Before Improvement Occurred	Result
8051	7	16	8	Cured
D. S.	12	16	5	Cured
J. deF.	1½	16	4	Cured
H. Z.	6	16	6	Cured
6851	12	16	4	Cured; sinus with an old discharge cicatrized
9783	3½	16	4	Cured
D. V.	9	16	5	Subsided but recurred later
9140	8	8	..	Treatment discontinued because of no effect; glands had disappeared 4 months later
9103	10	10	..	No improvement
8973	8½	16	..	No improvement
8464	13½	16	..	Slight improvement
F. L.	3½	4	..	No improvement
W. C.	10	12	..	No improvement
8575	3	16	..	Slight improvement
S. Z.	7	16	6	Improved

healed, but the disease recurred later. The conditions in the other eight were unaffected or advanced to a more severe type requiring surgical removal. Adenitis developed in two children who had previously been treated with antigen for other lesions. Both of these responded well to further administration of antigen. One child with a persistent discharge from a sinus resulting from an operation three years previously was cured of this discharge as well as of the recurrent adenitis.

Phlyctenular Conjunctivitis (Twenty-Seven Cases).—The patients with ocular involvement who were treated showed all degrees of phlyctenular conjunctivitis from a small phlyctenule in one eye to bilateral corneal ulceration. In every instance the reaction to the tuberculin test was positive, and other possible causative infections were excluded. Beneficial results were noted in all but one case. A cure resulted if the lesion was not so advanced that healing was impossible

5. Courcoux, A., and Biderman, A.: Semaine d. hôp. de Paris **3**:518 (Nov. 30) 1926; J. méd. franç. **16**:244 (June) 1927.

TABLE 2.—*Phlyctenular Conjunctivitis Treated with Antigen*

Case	Age	Mantoux Test	Lesion	Duration of Treatment, Weeks	Number of Doses Before Improvement Occurred	Result
9280	10	$\frac{15 \times 20}{40 \times 45}$	Bilateral conjunctivitis	16	?	Cured
8313	4	$\frac{10 \times 10}{30 \times 30}$	Corneal ulceration of both eyes; severe conjunctivitis	(1) 16 (2) 12	..	Quiescent after first 16 weeks, then lesion reactivated; cured after second 12 weeks of treatment
8476	6	$\frac{15 \times 15}{35 \times 40}$	Keratitis	(1) 16 (2) 16 (3) 16	..	Cured
8051	6	$\frac{10 \times 10}{70 \times 45}$	Severe conjunctivitis	16	3	Cured
6275	12	$\frac{25 \times 15}{30 \times 45}$	Bilateral corneal ulceration	(1) 16 (2) 16	..	Cured
9504	4½	Strongly +	Bilateral ulceration	16	4 or 5	Cured
B. R.	2½	Strongly +	Severe conjunctivitis	16	3	Cured
2572	13	$\frac{15 \times 15}{30 \times 30}$	Bilateral corneal ulceration	16	..	Cured
S. Z.	6	$\frac{25 \times 25}{50 \times 50}$	Severe conjunctivitis	16	4	Cured
6858	6	$\frac{12 \times 12}{40 \times 50}$	Mild conjunctivitis	16	3	Cured
7350	10	$\frac{10 \times 10}{25 \times 30}$	Severe keratitis	(1) 16 (2) 16	6	(1) Improved (2) Cured
7180	8	Strongly +	Conjunctivitis	16	4	Cured
A. L.	16 mo.	Strongly +	Bilateral ulceration	16	3	Cured
F. L.	5	25 × 25	Conjunctivitis	16	4	Cured
E. D.	7	$\frac{30 \times 35}{75 \times 100}$	Severe conjunctivitis	16	5	Cured
E. deF.	3	Strongly +	Severe conjunctivitis	16	4	Cured
M. F.	4	Strongly +	Severe conjunctivitis	(1) 16 (2) 16	4	(1) Improved (2) Cured
J. M.	5	Strongly +	Severe conjunctivitis	16	3	Cured
O. P.	3	Strongly +	Severe conjunctivitis	16	4	Cured
C. H.	5	20 × 30	Conjunctivitis	10	4	Improved, but stopped treatment
8135	11	Strongly +	Conjunctivitis	16	4	Cured
I. E.	10	Strongly +	Corneal ulcers	(1) 10 (2) 6 mos.	(1) 4 (2) 8	(1) Improved; stopped treatment (2) Much improved
W. S.	8	Strongly +	Severe conjunctivitis	10	5	Much improved
6890	6	$\frac{5 \times 5}{8 \times 60}$	Conjunctivitis	16	?	Cured
8308	3½	$\frac{10 \times 10}{30 \times 30}$	Conjunctivitis	16	5	Cured
8620	1¾	$\frac{5 \times 5}{30 \times 30}$	Conjunctivitis	16	..	Cured
6208	3	$\frac{10 \times 10}{20 \times 30}$	Conjunctivitis	16	?	Cured

without the production of scar tissue. The improvement was usually rapid and lasting after one course of treatment. After three or four doses, most of the acute symptoms and signs were gone. In severe ulcerative cases further destruction was prevented and relief afforded from the acute symptoms. Indeed, the reduction of the disability from which some of these children suffered was so great that the results are regarded as the restoration of sight to the blind, a result which all manner of local applications previously used over long periods had failed to achieve. Three such children prior to taking the antigen were forced by their defective eyesight to attend sight-saving classes. Subsequent to treatment they were able to go to ordinary schools. In the only case in which the condition proved resistant to protracted and intensive treatment, in that the acute symptoms disappeared but a nodule thought to be tuberculous remained in the fundus, the eye was removed because of the proximity of the supposed tuberculoma to the optic disk. Sections of

TABLE 3.—*Tuberculosis of the Bone and Skin Treated with Antigen*

Case	Age	Lesion	Duration of Treatment	Number of Doses Before Improvement Occurred	Result
4919	10	Dactylitis.....	6 mos.	3 mos.	All but one finger cured
8790	18 mos.	Dactylitis.....	6 mos.	4 mos.	Cured
M. F.	5	Persistent sinus from tuberculous ankle	16 wks.	6 wks.	Cured
R. M.	7	Multiple tuberculous osteomyelitis and skin tuberculosis	8 mos.	3 mos.	Cured
I. W.	13	Ulceration on thigh present for 12 years	6 mos.	4 wks.	Cured
L. B.	11	Necrotic lesion of nose.....	2 mos.	6 wks.	Slight improvement

the eye showed the nodule to be purely fibrous. The results suggest that methylated antigen acts as a specific for any child with keratitis with a positive reaction of tuberculin.

Tuberculosis of the Bone (Four Cases).—The cases of tuberculosis of the bone in which treatment was given consisted of two cases of multiple tuberculous dactylitis, two of chronic discharge from the sinuses of old bone lesions and one of multiple tuberculous osteomyelitis. The dactylitis responded very slowly to treatment. In one child the lesion on the finger most affected broke down, and the finger had to be amputated. The others eventually healed completely. The discharge from the sinuses quickly healed. The patient with multiple bone lesions was a child of 7 who for years prior to treatment had had foci break out in many places. One lesion no sooner subsided than another appeared. *Bacillen* emulsion had previously been tried without success. After a protracted course of antigen all the bone lesions healed, and no new foci have appeared within nearly three years since the completion of treatment. There previously were frequent periods in which the

mediastinal lesion had become active. No signs or symptoms suggestive of such activity have been seen in the past three years, and the child has remained continuously well and able to attend school.

Tuberculosis of the Skin (Two Cases).—The French workers claim to have obtained good results with the use of antigen in tuberculosis of the skin. Only two such patients presented themselves at our clinic. One of these had an extensive necrotic lesion on her nose. This lesion dried up considerably after a few treatments, but a complete course of treatment was not given, as the child failed to return. The other patient, a boy aged 13, had extensive lesions on the thigh, which had been variously treated since he was 6 months of age. The lesion had continued to spread slowly and to discharge foul-smelling material. The ulcer healed after a few doses of antigen were given, and in a few months the area was covered with thin new skin. No evidence of spread or of breaking down has been apparent in the past year since the first course of antigen was given.

Asthma (Two Cases).—Two children sensitive to tuberculin who had severe asthma were much improved by a course of antigen.

CONCLUSION

Methylated antigen offers possibilities of successful treatment in certain types of external tuberculosis. The most striking results are obtained in cases of phlyctenular conjunctivitis associated with tuberculous infection, but this treatment offers sufficient hope of success in cases of tuberculosis of the bone, skin and glands to merit a fair trial in these cases.

HISTAMINE TEST OF GASTRIC SECRETION

WITH PARTICULAR REFERENCE TO ITS PRACTICABILITY IN CHILDHOOD; A PRELIMINARY COMMUNICATION

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While preparing for work on another problem it was decided to employ the histamine test of gastric secretory function as a part of the study. A search for data concerning the use of the test in children yielded only a few references and revealed the desirability of work on the subject. Literature on the histamine test in the adult is copious. According to Lee,[1] the test resulted as a development of work by Dale and Richards in 1918 and of Popielski in 1920. Bockus and Bank[2] accredit Carnot, Koskowski and Liebert with the first observation regarding the effect of histamine on the human stomach. Since its introduction as a test of gastric secretory function, the histamine test has enjoyed great vogue. The enthusiasm with which the test was heralded and accepted is, no doubt, an expression of a widespread recognition of inaccuracy and inadequacy of the gastric function tests that had been employed previously. Bloomfield and Polland[3] criticized the test meal on the grounds that: (1) appetite, distaste for food, rapidity of eating and varying quantities of saliva give rise to inconstant results; (2) the test meal is not a maximum stimulus to gastric secretion and cannot be repeated with identical results; (3) the material tested consists of a mixture of secretions and test meal, and not of gastric juice; (4) the emptying rate of the stomach influences the results; (5) only a general idea regarding the volume of gastric juice secreted is gained. These criticisms seem to be met to a large extent by the histamine test. In adults the test has been found of great value in differentiating between pseudo-achylia and true achylia.

Histamine (*B*-iminazolylethylamine) is a derivative of the amino-acid histidine, which, according to Sollmann,[4] occurs in all tissues.

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1. Lee, F. C.: One of the Newer Methods for the Study of Gastric Function, Internat. S. Digest **8**:323, 1929.

2. Bockus, H. L., and Bank, J.: The Value of Histamine as a Test for Gastric Function, Arch. Int. Med. **39**:508 (April) 1927.

3. Bloomfield, A. L., and Polland, W. S.: The Diagnostic Value of Studies of Gastric Secretion, J. A. M. A. **92**:1508 (May 4) 1929.

4. Sollmann, T.: A Manual of Pharmacology, Philadelphia, W. B. Saunders Company, 1926.

Although histamine is found in relatively large amounts in the normal gastro-intestinal tract, it is destroyed at this site and is therefore ineffective when administered by mouth. Subcutaneous or intramuscular injection of the drug in sufficient amount is followed by capillary dilatation, lowering of blood pressure and stimulation of many secretory glands. Excessive doses produce a condition similar to that of anaphylactic shock. Rühl,[5] working with animals, found doses of 1 mg. per kilogram to produce severe myocardial damage with cardiac dilatation and increased resistance in the pulmonary circulation. Bally[6] pointed out that in the rabbit, in accordance with its known property of stimulation of smooth muscle, histamine produces a rise in blood pressure (presumably due to vasoconstriction). Rabbits dying of histamine shock show engorgement of the right side of the heart. Dobson[7] advised using the drug cautiously in cardiac and asthmatic cases because of the reported constrictive action on the bronchioles. Sollmann[4] is of the opinion that histamine is probably closely related to gastrin or secretin. Both Sollmann[4] and Cushny[8] stated that it stimulates the secretion of saliva and of gastric and pancreatic juices. Lim, Matheson and Schlapp,[9] however, concluded that when gastric juice is prevented from entering the duodenum stimulation of pancreatic and biliary secretions does not occur.

All workers are agreed that histamine is a strong stimulus to gastric secretion. However, Babkin,[10] in contradistinction to the views held by other authors, contended that histamine is a selective or partial stimulus for gastric secretion. He stated that at least two kinds of stimuli play a rôle in the gastric secretory function, namely, (1) nervous and (2) humoral or hormonal. Histamine is regarded as a humoral stimulus, which stimulates chiefly the parietal cells of the gastric glands, the function of which cells is the production of fluid, hydrochloric acid, and some other inorganic constituents. The activity of these cells is

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5. Rühl, A.: Ueber Herzinsufficienz durch Histamin, Arch. f. exper. Path. u. Pharmakol. **145**:255, 1929.

6. Bally, L. H.: Studies on Histamine Reactions in Rabbits, J. Immunol. **17**: 191, 1929.

7. Dobson, H. V.: Effect of Histamin on Gastric Secretion: With Especial Reference to Achlorhydria: Preliminary Report, J. A. M. A. **84**:158 (Jan. 17) 1925.

8. Cushny, A. R.: Pharmacology and Therapeutics, Philadelphia, Lea & Febiger, 1928.

9. Lim, R. K. S.; Matheson, A. R., and Schlapp, W.: A New Duodenal Technique, Edinburgh M. J. **30**:265, 1923.

10. Babkin, B. P.: The Value of Histamine as a Test of Gastric Secretion from a Physiological Standpoint, Canad. M. A. J. **23**:268, 1930; Address on Factors Regulating Composition of Gastric Juice, ibid. **25**:134, 1931.

also influenced by the nerve supply, chiefly the parasympathetic nerves. The cells responsible for the production of the organic and enzymic portions of gastric juice are said to be almost exclusively under control of the parasympathetic nerve supply. Stimulation of the parasympathetic nerve of a dog with a Haidenhain pouch with pilocarpine was found to increase the peptic activity of gastric juice strikingly, while histamine caused no active production of enzymes. Histamine, moreover, was found to produce what the author stated might be described as a "washing out" process in its effect on the secretion of organic and enzymic portions of the juice. He concluded that "in judging the value of histamine as a test for gastric secretion, it may thus be said that histamine is a good stimulus for the production of acid gastric juice. Histamine gastric juice is poorer in organic substances than juice activated by the ingestion of food," and he stated that an attempt was being made to combine the histamine and pilocarpine stimulation of gastric juice in dogs.

In addition to its partial stimulation of gastric juice, histamine apparently may influence the secretion of the components of the inorganic or chloride portion of the gastric juice differently. As a rule, the fasting gastric content is low in free hydrochloric acid and combined acidity, whereas it is relatively high in total chlorides. The neutral chloride portion (difference between free hydrochloric acid and total chloride) has commonly been assumed to be the result of neutralization of hydrochloric acid. Recent workers have, however, been impressed more and more by the possibility of a separate secretion of neutral chloride. Roberts [11] expressed the belief that the chloride ion may be secreted as inorganic chloride along with hydrochloric acid, and he stated that Katsch and Kalk also concluded that there is a secretion of chloride independent of that of acid. Duthie [12] called attention to the fact that Maclean and his colleagues have demonstrated the secretion of the chloride ion partly as hydrochloric acid and partly as sodium chloride. Steinitz [13] was emphatic in his contention that hydrochloric acid and neutral chloride are secreted independently. The mechanism of hydrochloric acid secretion is said to be delicate and more readily influenced than is the neutral chloride secretory mechanism. Observations by Berglund,[14] who studied the influence of fever on

11. Roberts, W. M.: The Fasting Gastric Secretion in Man, Quart. J. Med. **21**:7, 1927.

12. Duthie, R. J.: The Action of Histamine on the Chloride Content of the Stomach, Quart. J. Med. **23**:447, 1930.

13. Steinitz, H.: Die Chlorabscheidung des mensclichen Magens in ihren Beziehungen zu pathologischen Vorgängen, Arch. f. Verdauungskr. **42**:57, 1928.

14. Berglund, H.: Unpublished data.

gastric secretion, and by Berglund and Chang [15] tend to support this contention. The work of both Steinitz [13] and Duthie [12] points toward a relatively greater stimulation of hydrochloric acid than of neutral chloride in the normal person. In abnormal cases the secretion of hydrochloric acid may fail to respond, while the total chloride secretion increases markedly.

The dosage employed in work on adults has varied considerably, some authors using an arbitrary dose of 0.5, 1, 1.5 mg. or more, others basing the dosage on body weight. Bloomfield and Polland [3] regarded 0.01 mg. per kilogram as adequate, and stated that it produces no unpleasant results. Gompertz and Cohen,[16] comparing the effects of doses of 1, 0.75, 0.5 and 0.25 mg., concluded that 0.25 mg. is a sufficiently large dose to stimulate gastric secretion; they found no untoward results from its use. Lee [1] endorsed smaller doses, regarding 0.0017 mg. per pound (0.0037 per kilogram) as adequate. He quoted Rothlin and Gundlach (working with a Pavlov pouch) as having found 0.0033 per kilogram effective.

Coari,[17] working with children ranging in age from less than 6 months to 5 years, used doses of from 0.25 to 1 mg., but he reported undesirable results. Dietrich and Shelby [18] quoted Harmelin as finding 0.05 mg. per kilogram necessary for maximum gastric secretion after three hours. They themselves used 0.01 mg. per kilogram in three children 4 years old, and a dose of 0.25 mg. for ten children ranging in age from 7 to 12 years, and in weight from 47 to 89 pounds (21.3 to 40.4 Kg.).

In addition to the variations in dosage employed, one is confronted with the variation in preparations used. Different salts of the histamine base vary in physiologic activity, depending on the weight of the molecule with which histamine is combined. Thus, according to information furnished by Burroughs Welcome and Company, histamine dihydrochloride contains 60 per cent and histamine acid phosphate contains 36 per cent histamine base.

EXPERIMENTAL WORK

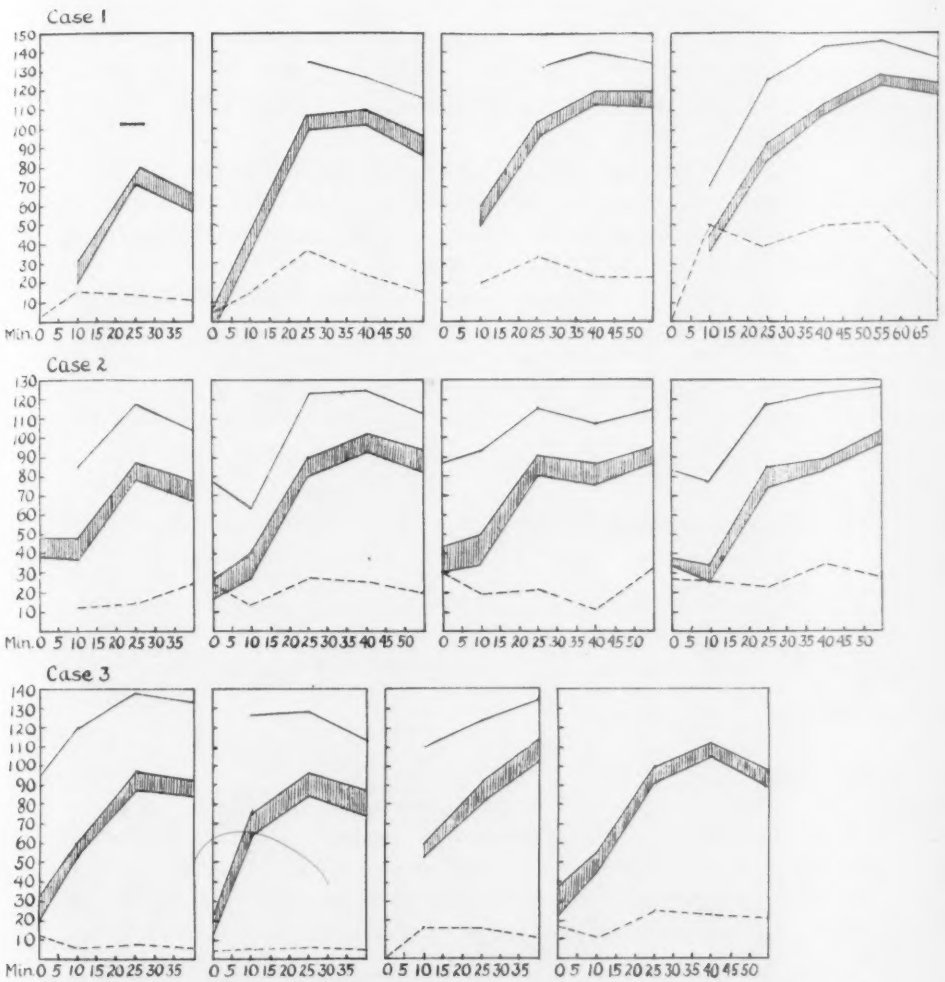
The object of the experimental work was mainly to establish, if possible, an optimum dosage of histamine for children, to determine

15. Berglund, H., and Chang, H. C.: Transitory Character of Achlorhydria During Fever Demonstrated by Histamine Test, Proc. Soc. Exper. Biol. & Med. **26**:422, 1929.

16. Gompertz, L. M., and Cohen, W.: The Effect of Smaller Doses of Histamine in Stimulating Gastric Secretion, Am. J. M. Sc. **177**:59, 1929.

17. Coari, A.: Histamine Test in Children, Pediatria **35**:365, 1927.

18. Dietrich, H., and Shelby, D. C.: Gastric Analysis in Childhood, Am. J. Dis. Child. **41**:1086 (May) 1931.



Gastric response to histamine in varying dosages. The volume, expressed in cubic centimeters, is represented by the broken line. The free hydrochloric acid and total acidity, expressed in tenth-normal cubic centimeters per hundred cubic centimeters of gastric juice, are represented by the shaded area (free hydrochloric acid lower limit; total acidity upper limit). The total chlorides, expressed in tenth-normal cubic centimeters per hundred cubic centimeters of gastric juice, are represented by the continuous line.

the feasibility of, and to develop a more or less standard procedure for, fractional analysis and a single aspiration test.

Histamine acid phosphate, which is supplied in hypodermic tablets each containing 0.003 Gm. of histamine acid phosphate or the approximate equivalent of 0.001 Gm. of histamine base, was used. Since one tablet dissolved in 1 cc. of water forms a 1:1,000 solution this is a convenient form of the drug.

Children in the pediatric and orthopedic services of the University of Chicago clinics were used as subjects. Although most of the children were not entirely normal, the majority of them were not acutely ill and at least approached the normal condition.

As one phase of the work results with doses of 0.0025, 0.005, 0.01 and 0.02 mg. (histamine base) per kilogram of body weight were compared regarding the effect on gastric secretion and the extragastric effects. To meet the criticism that results of an initial test may be lower than those of a subsequent test, the test with the 0.0025 mg. dose was repeated after completion of the series of tests, with closely similar results in cases 1 and 3 (table 1). In case 2 the results of the last examination were about 30 or 40 per cent greater than on the first examination. In the accompanying chart and table 1 results of the last test, with 0.0025 mg. in cases 1 and 2, are recorded.

TABLE 1.—*Extragastric Reactions with Varying Doses of Histamine*

No.	Dose, Mg. per Kg. of Body Weight	Maximum Blood Pressure Decrease, Mm. Hg		Maximum Pulse Rate Acceleration, Beats in 1 Min.	Skin Reaction			Other Symptoms
		Systolic	Diastolic		Local	Face	Other Parts	
1	0.0025	2	14	20	++	+++	+	Headache
	0.005	0	12	28	+++	+++	++	Headache
	0.01	12	22	20	+++	+++	+++	
	0.02	14	22	42	+++	++++	+++	Headache, vertigo, crying
2	0.0025	4	4	8	++	+++		
	0.005	?	4	24				
	0.01	0	14	32	++	++++	++	
	0.02	10	38	46	+++	++++	+++	Headache, vertigo, crying; body vibrating with pulse
3	0.0025	0	0	0	++	++		
	0.005	8	8	12	++	++		
	0.01	14	22	16	++	+++	+	
	0.02	16	24	42	++	+++	++	

All tests reported, with the exception of one, as indicated in table 2, were carried out on a fasting stomach in the morning. Keller and Molner [19] reported a diurnal variation in gastric response and expressed the belief that the greatest response occurs at the time of day at which the subject is accustomed to taking the largest meal. A few tests were

19. Keller, F., and Molnar, A. L.: Ueber die Tagesschwankungen der Magensekretion und über ihre klinische Bedeutung, Arch. f. Verdauungskr. **41**:262, 1928.

TABLE 2.—*Results of Fractional Gastric Analysis*

No.	Sex; Age, Years	Wt., Kg.	Clinical Status	Specimen	Bile	Mucus	Volume, Cc.	Free Hydrochloric Acid*	Total Acid*	Total Chloride*	Comment
1	F 10	25	Undernutrition; mother had pernicious anemia	Fasting	..	++	15.0	...	...	...	
				10 min.	—	+	32.0	0	4	30	
				25 min.	—	+	28.0	0	6	31	
				40 min.	—	+	20.0	0	6	40	
				55 min.	—	+	15.0	0	6	45	
2	M 12	30	Undernutrition; mother had pernicious anemia	Fasting	..	..	10.0	...	...	...	Test done in the afternoon
				10 min.	—	++	25.0	8	17	68	
				25 min.	—	±	40.0	51	63	89	
				40 min.	—	—	32.0	38	48	75	
				55 min.	—	+	29.0	21	29	48	
				70 min.	—	—	16.0	21	84	43	
				85 min.	—	—	19.0	25	36	22	
3	F 10	24	Anorexia nervosa	10 min.	—	++	19.0	17	27	55	
				25 min.	—	±	142.0	77	84	100	
				40 min.	—	+	50.0	61	65	93	
				55 min.	—	++	15.0	12	19	40	
4	F 11	31	Calcifying hilus tuberculosis; chronic uveitis; undernutrition	10 min.	—	+	4.5	32	40	...	
				25 min.	—	+	5.0	46	59	...	
				40 min.	+++	++	14.5	61	70	118	
				55 min.	+	+	22.0	86	93	117	
				70 min.	++	+	14.0	72	80	102	
5	M 11	..	Compensated rheumatic heart disease; myopia; chorioiditis; undernutrition	Fasting	—	±	25.0	61	72	123	
				10 min.	—	±	21.0	91	101	141	
				25 min.	—	—	41.0	125	131	150+	
				40 min.	—	—	31.0	129	135	150+	
				55 min.	—	—	30.0	133	138	150	
				70 min.	—	—	25.0	129	135	150	
6	F 12	44	Convalescing from subchronic nephritis; maxillary sinusitis	10 min.	±	±	25.0	48	57	115	
				25 min.	—	—	55.0	107	113	145	
				40 min.	—	—	38.0	128	134	150	
				55 min.	—	+	23.0	126	132	149	
				70 min.	—	+	12.0	92	99	141	
7	F 12	34	Undernutrition	Fasting	—	++	15.0	0	8	...	Trace of blood in 40 and 55 minute specimens
				10 min.	—	±	11.0	48	63	125	
				25 min.	—	—	17.0	122	130	150	
				40 min.	—	—	18.0	136	143	150	
				55 min.	—	—	5.0	130	138	...	
8	M 11	25	Recurrent attacks of headaches and vomiting; undernutrition	Fasting	—	++	6.0	0	10	...	
				10 min.	—	+	40.0	25	36	87	
				25 min.	—	—	50.0	90	99	124	
				40 min.	+	—	40.0	94	103	126	
				55 min.	++	+	25.0	94	103	118	
				70 min.	++	++	9.0	67	75	...	
9	F 12	47	Convalescent from acute nephritis	Fasting	—	++	26.0	29	40	110	
				10 min.	—	+	22.0	44	54	105	
				25 min.	—	+	30.0	67	75	123	
				40 min.	—	±	24.0	78	88	126	
				55 min.	—	±	26.0	82	90	125	
				70 min.	+	+	24.0	69	78	124	
10	F 11	40	Recurrent acute abdominal pain; roentgen evidence of duodenal ulcer ?	Fasting	—	±	5.0	38	54	...	About 30 cc. vomited while passing tube
				10 min.	—	—	0.0	...	...	...	
				25 min.	—	++	13.0	42	50	...	
				40 min.	—	+	42.0	52	59	97	
				55 min.	—	+	34.0	55	65	98	
				70 min.	—	+	40.0	36	46	63	
11	F 9	28	Chronic arthritis (rheumatic ?); iridocyclitis	Fasting	—	+	7.0	6	26	...	
				10 min.	—	±	21.0	47	64	125	
				25 min.	—	—	33.0	111	117	150	
				40 min.	—	—	28.0	137	139	150—	
				55 min.	—	—	22.0	137	141	150—	
				70 min.	++	—	10.0	133	139	145	
12	F 10	26	Abdominal pain (cause undetermined)	Fasting	++	+	14.0	32	43	...	
				10 min.	+	—	16.0	75	81	...	
				25 min.	—	—	26.0	120	124	149	
				40 min.	—	—	28.0	150	154	150	
				55 min.	+	—	32.0	113	118	150	
				70 min.	++	+	5.0	115	120	...	

* Free hydrochloric acid, total acidity and total chlorides are expressed in tenth-normal cubic centimeters per hundred cubic centimeters of gastric juice.

TABLE 2.—*Results of Fractional Gastric Analysis—Continued*

No.	Sex; Age, Years	Wt., Kg.	Clinical Status	Specimen	Bile	Mucus	Volume, Cc.	Free Hydrochloric Acid*	Total Acid*	Total Chloride*	Comment
13	F 12	35	Epigastric pain after eating; flatulence; loss of weight; chronic articular rheumatism	Fasting	+	+	9.5	38	49	...	
				10 min.	±	++	28.0	32	41	108	
				25 min.	—	—	23.0	70	79	132	
				40 min.	—	++	24.0	92	98	142	
				55 min.	—	++	8.0	102	109	...	
14	M 10	28	Epigastric pain after eating; questionable roentgen evidence of gastritis and ulcer	Fasting	—	±	15.0	62	70	118	
				10 min.	—	±	11.0	62	73	119	
				25 min.	—	+	41.0	75	83	127	
				40 min.	—	+	28.0	79	90	122	
				55 min.	—	++	15.0	60	70	118	
15	F 14	44	Functional (?) heart disturbance	Fasting	++	+	23.0	23	36	91	Trace of blood in 40 and 55 minute specimens
				10 min.	—	++++	24.0	0	15	66	
				25 min.	—	+	44.0	79	88	123	
				40 min.	—	—	25.0	105	111	143	
16	F 11	26	Low back pain; abdominal pain (cause undetermined)	Fasting	—	±	28.0	30	45	93	Trace of blood in 55 minute specimen
				10 min.	—	—	18.0	51	64	102	
				25 min.	—	—	34.0	77	90	111	
				40 min.	—	—	24.0	85	96	116	
				55 min.	—	+	19.0	53	62	89	
17	F 11	..	Late poliomyelitis; paralysis	Fasting	—	++	2.0	0	2	...	Uncooperative; histamine, about 0.007 mg. per Kg.
				10 min.	..	++++	45.0	0	11	64	
				25 min.	..	+++	21.0	28	39	83	
				40 min.	..	++++	17.0	13	23	63	
18	F 10	48	Muscular dystrophy	10 min.	—	+	19.0	51	61	...	
				25 min.	—	+	34.0	98	104	132	
				40 min.	—	±	24.0	114	120	140	
				55 min.	—	±	24.0	112	120	134	
19	F 12	48	Idiopathic scoliosis; healing juvenile pulmonary tuberculosis	Fasting	++	±	30.0	31	43	88	
				10 min.	+	±	25.0	26	39	93	
				25 min.	+	+	27.0	81	91	117	
				40 min.	—	+	11.0	77	87	109	
				55 min.	±	±	33.0	87	95	117	
20	F 10	27	Congenital dislocation of hips	10 min.	+	+	17.0	53	59	110	Trace of blood in 25 and 40 min. specimens
				25 min.	±	±	17.0	83	91	124	
				40 min.	±	±	11.0	104	112	130	

* Free hydrochloric acid, total acidity and total chlorides are expressed in tenth-normal cubic centimeters per hundred cubic centimeters of gastric juice.

performed during the afternoon and compared with tests done during the forenoon. The results were almost identical. It was found that at least six hours should elapse between the time of the last meal and the time of the test, because of the difficulty usually encountered when the stomach contains small amounts of food.

In the case of tests of fractional analysis after the subject is made comfortable in bed (trunk inclined about 30 degrees) and has been told calmly what is about to take place and advised how to conduct himself, the blood pressure and pulse rate are determined, and the tube is introduced into the stomach. A duodenal tube of rather small caliber (size 14 F.) without a metal tip but with several perforations near its termination was used. As a rule little difficulty is encountered. If the child is particularly obstreperous, the tube may be introduced via the nose. This was found necessary in only one case. The distance

that a tube must be introduced varies, of course, with different children and with the position of the stomach. If the tube is manipulated and if fasting content is present, the most dependent portion of the stomach is usually found fairly readily. Although Duthie [20] and Butcher [21] reported variations in free hydrochloric acid and total chloride in the upper and lower portions of the stomach, the variations are probably not extremely significant. Since the tube may not remain at the same level, anchoring to the face with adhesive tape is an aid. All the fasting content of the stomach is aspirated, and the subject is instructed to expectorate all the saliva. The histamine (routine dose 0.01 mg. per kilogram) is then injected subcutaneously, and in addition to the aspirations, observations on changes in blood pressure and pulse rate and on external effects of the histamine are made. Usually within a few minutes after injection a flushing of the face and neck, reddening and wheal formation at the site of injection, a moderate decrease in blood pressure and a moderate acceleration of the pulse rate occur. Later a generalized erythema may be observed. A further decrease in blood pressure (maximum average about 7 mm. of mercury systolic and about 20 mm. of mercury diastolic) and a further acceleration of pulse rate (maximum average about 30 beats per minute) occur. At times the subject complains of a headache. These signs and symptoms reach their peak, on the average, about from eight to twenty minutes after injection and tend to abate completely by the end of one hour. The stomach is aspirated ten minutes after the injection and every fifteen minutes thereafter over varying periods of time. If practically no fluid is obtained, one should make sure that the subject is not biting the tube. Mucus may obstruct the tube and can be expelled by injecting a small amount of air into the stomach. At times manipulation of the tube may yield results. Strong suction should be avoided, because only moderately strong suction may injure the gastric mucosa and lead to slight bleeding. The fluid obtained is, as a rule, almost clear, at times presenting a cloudy or flaky appearance. Mucus in varying amounts is usually present. Bile may be present. The specimens were placed in the refrigerator and were examined within a few hours after the test. Copeman and Hill [22] reported variations in results with time of titration. However, they worked with the test meal and did not state the temperature at which the specimens were kept. Carlson [23] has shown

20. Duthie, R. J.: Variation in Free Hydrochloric Acid and Total Chloride in the Upper and Lower Parts of the Stomach, Quart. J. Med. **22**:575, 1929.

21. Butcher, quoted by Copeman, W. S. C., and Hill, N. G.[22]

22. Copeman, W. S. C., and Hill, N. G.: The Clinical Application of Total Chloride Estimations in the Fractional Test Meal with an Analysis of a Series in Fifty Normal Children, Quart. J. Med. **23**:33, 1928.

23. Carlson, A. J.: The Control of Hunger in Health and Disease, Chicago, University of Chicago Press, 1916.

that autolysis of gastric juice occurs at a temperature of 38 C. In two cases determinations made within a few hours after completion of the test and after twenty-four hours yielded identical results. Evidently specimens may be kept at low temperatures over long periods of time

TABLE 3.—*Results of Single Aspiration Tests*

No.	Sex; Age, Years	Wt., Kg.	Clinical Status	Bile	Mucus	Volume, Cc.	Free Hydrochloric Acid*	Total Acid*	Total Chloride*	Comment
1	M 5½	27	Recurrent abdominal pain	—	—	....	71	80	106	
2	F 12	44	Convalescing from subchronic nephritis	—	—	55.0	115	122	150+	0.005 mg. of histamine per Kg.
3	M 1	6	Malnutrition	—	++	4.5	48	59	...	
4	F 8	20	Chronic pneumonia; undernutrition; anorexia	—	++	15.0	73	85	118	
5	M 9	24	Abdominal pain after eating	—	+	35.0	90	100	130	About 15 cc. vomited
6	F 5	16	Anorexia nervosa; nervous vomiting	—	++	12.0	88	96	136	
7	F 6½	19	Anorexia nervosa; nervous vomiting	+	+	22.0	75	87	118	
8	F 6½	19	Nervous child; undernutrition	±	+	30.0	85	94	121	
9	M 13	33	Mild chronic colitis	±	+	29.0	102	112	145	0.016 mg. of histamine per Kg.
10	F 13	48	Idiopathic scoliosis; healing juvenile pulmonary tuberculosis	+	±	67.0	87	95	128	Trace of blood
11	F 10	48	Muscular dystrophy	—	±	51.0	93	102	130	
12	F 10	27	Congenital dislocation of hips	+	+	....	53	61	104	
13	F 6	23	Chronic maxillary sinusitis; morning vomiting	—	±	6.0	81	89	120	
14	M 13	33	Nervous child	—	±	45.0	85	93	118	Trace of blood
15	F 10	27	Chronic constipation; vague abdominal pain; anorexia	±	±	38.0	75	83	109	
16	F 6	19	Enuresis	—	±	31.0	93	102	134	About 20 cc. vomited
17	M 4½	21	Epilepsy	+	+	....	37	47	...	
18	M 9	24	Arthritis	±	±	23.0	71	77	115	
19	M 11	24	Arthritis	—	+	....	49	61	106	
20	F 9	30	Late poliomyelitis; paralysis	—	++	5.0	20	28	78	Aspiration difficult; vomiting

* Free hydrochloric acid, total acidity and total chlorides are expressed in tenth-normal cubic centimeters per hundred cubic centimeters of gastric juice.

without the occurrence of titrable changes. After standing for a short time, the mucus separates from the rest of the specimen and by careful manipulation of the pipet a sample of nearly pure gastric juice can be obtained, thus rendering filtration unnecessary. If the specimen is small, it is difficult to avoid admixture of mucus. Specimens of 5 cc. were used whenever possible. Smaller specimens yield somewhat less accurate

results. Titrations for free hydrochloric acid and total acidity were made with tenth-normal sodium hydroxide, dimethylamino-azobenzene (Toepfer's reagent) and phenolphthalein being used as indicators. Determinations of the total chloride were made by the Van Slyke [24] method.

Although the fractional analysis method of examination is, no doubt, of greater value than is a single aspiration method in determining gastric secretory function, especially for experimental purposes, it is probably, as Chang [25] pointed out, "not at all necessary" for clinical purposes. Berglund and Chang [15] aspirated the fasting content of the stomach and repeated the aspiration twenty minutes after the injection of histamine. Steinitz [13] referred to the single aspiration test as a "Stichprobenausheberung." He made aspirations from twenty-five to thirty-five minutes after the injection of histamine. The advantage of a single aspiration test per se and its advantage over a single aspiration test meal especially in children are, of course, obvious. Anorexia or distaste for the test meal may influence the results decidedly. In the case of a child, the meal may be refused. If the fasting stomach content is not aspirated and if the subject is not familiar with the single aspiration test procedure, the possible inhibition by fear of the test can be eliminated almost entirely. Table 3 contains the results of single aspiration tests for specimens aspirated from thirty to forty minutes after injection of histamine (0.01 mg. per kilogram), no aspiration of the fasting content having been made.

COMMENT ON RESULTS

Considering the comparative effects of various doses as recorded in the accompanying chart and table 1, it is evident that the curves in cases 1 and 2 resemble each other most closely. The two subjects resembled each other clinically also. They were well nourished or overnourished, whereas the subject in case 3 was undernourished. The cases are represented by numbers 18, 19 and 20 in table 2. While it is true, as Gomperts and Cohen [16] found, that gastric response is not mathematically proportional to the dose of histamine, there is, nevertheless, a definite variation in response with variation in dosage. With smaller doses, the peak of acidity and total chloride is reached earlier than with larger doses. The varying reports of different authors regarding the time of maximum response after stimulation with histamine can probably be explained largely on the basis of variations in the size of the doses used. The curves for the free hydrochloric acid and total acidity show a

24. McLean, Hugh: Modern Views on Digestion and Gastric Disease, New York, Paul B. Hoeber, Inc., 1926, p. 128.

25. Chang, H. C.: Gastric Analysis by the Histamine Method, Nat. M. J. China **16**:59, 1930.

remarkable parallelism. In agreement with the findings of Chang,[25] the values for combined acidity do not as a rule exceed those for free hydrochloric acid by more than from 10 to 15 cc. The curve for total chloride parallels that for the acidity quite closely. This finding is in agreement with that of Chang,[25] Roberts [11] and Bloomfield and Polland.[3] While the curve for the volume also varies to some extent with the size of the dose, the statement of Dobson [7] that the increase in the concentration of acid following stimulation with histamine is relatively greater than the increase in volume is apparently confirmed. In contradistinction to the report of Gompertz and Cohen,[16] who stated that variations in dosage do not give rise to any appreciable difference in pulse rate or blood pressure, but that the external manifestations present marked differences, it was found that the pulse rate and blood pressure as well as external signs were more or less proportional to the size of the dose. In cases 1 and 2 the largest dose apparently gave rise to discomfort; the children became uneasy and cried. These symptoms were not observed in the other child, who was undernourished. Since the secretory curves also differ, the question arises whether the state of nutrition plays a rôle in the response to histamine. If this were the case, calculation of dosage on the basis of body weight would be complicated.

The results of fractional gastric analyses permit only more or less general statements. As was found in the curves in the accompanying chart, the values for free hydrochloric acid and total acidity bear a fairly intimate relationship to each other, and the total acidity is usually not more than 10 cc. in excess of the free hydrochloric acid. The values for free hydrochloric acid, combined acidity and total chlorides cannot be compared with those reported for test meals. With histamine, relatively pure gastric juice is obtained. As was pointed out by Carlson,[23] "normal human gastric juice is equivalent in total acidity to the maximum acidity reported by clinical observers for so-called hyperacidity in man." He stressed the importance of the rate of secretion and stated that the more rapid the rate of secretion the greater the values for acidity and total chloride. He expressed the belief that rapid secretion or disturbance of the neutralizing mechanism (as pyloric obstruction) may cause so-called hyperacidity. It is true that mucus, saliva in varying amounts (even though most of it is expectorated), secretions from the pharynx and mouth, which according to Carlson [26] may be surprisingly great in amount, and duodenal secretions and bile dilute and modify the constituency of gastric juice, and may account for low values in normal persons. Nevertheless, it seems likely that not all normal persons secrete gastric juice of maximum acidity. Difficulties in interpre-

26. Carlson, A. J.: Unpublished data.

tation of values are, of course, evident. No attempt will be made to classify the cases reported into the usual groups, achlorhydria, hypochlorhydria, normal acidity and hyperchlorhydria. Future work may make this possible. It is interesting to note that in the case of a child whose mother has pernicious anemia no free hydrochloric acid was secreted. A subsequent examination likewise proved negative for free hydrochloric acid. Some of the children had had previous experience with the tube (gastric motility tests, and in one case an Ewald test). It is possible that the subsequent results of gastric analysis are higher than they would have been on initial experience with the tube. Repeated tests are too few in number to warrant any definite statement regarding comparative results. The volume of gastric juice secreted varies greatly. In some cases it is enormous. Bloomfield and Polland [3] laid great stress on the volume secreted as an indication of secretory function.

TABLE 4.—*Comparison of Acidity and Chloride Values at Forty Minutes and with Single Aspiration Test at from Thirty to Forty Minutes*

	Fractional Gastric Analysis			Single Aspiration		
Number	Free Hydrochloric Acid*	Total Acid*	Total Chloride*	Free Hydrochloric Acid*	Total Acid*	Total Chloride*
1	114	120	139	115	122	150
2	114	120	140	93	102	130
3	77	87	109	87	95	128
	(55 min.) 87	(55 min.) 95	(55 min.) 117			
4	104	112	130	53	61	104

* Free hydrochloric acid, total acidity and total chlorides are expressed in tenth-normal cubic centimeters per hundred cubic centimeters of gastric juice.

Results of single aspiration tests indicate the practicability of this test. Even in cases of small volume and admixture of mucus values for acidity may be fairly high. In two of the cases recorded in table 4, single aspiration values are practically identical with those of fractional analysis. In the other two cases, there is considerable difference. In view of the fact, as is evident from table 2, that maximum values are not attained until the end of forty or fifty-five minutes, it might be advisable to aspirate forty-five minutes after the injection of histamine.

CONCLUSIONS

1. The gastric response to histamine varies with the size of the dose.

2. For comparative results, similar doses must be employed.

3. The optimum dosage for children apparently lies between 0.005 and 0.01 mg. per kilogram.

4. Fractional analysis by the histamine method is feasible and practicable in childhood.

5. The single aspiration test is distinctly advantageous for practical clinical purposes.

OCULAR TORTICOLLIS IN CHILDREN

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Tilting of the head in children is surprisingly frequent. It is only in cases in which the condition is marked that it is referred to as torticollis (L. tortus, twisted + collum, neck).

The causes of head tilting are varied and unrelated. Torticollis, or muscular wry neck (English)—*der Schiefhals* or *caput obstipum* (German), *cou tors* or *cou tortu* (French) and *torticollo* (Italian)— is congenital or acquired. In the congenital type the infant at birth or soon thereafter holds the head tilted toward one shoulder and the face turned toward the opposite one. The inclination cannot be overcome voluntarily. Examination frequently discloses a painless contracture of the sternocleidomastoid muscle on one side.

An extensive literature has grown up concerning the etiology of this form of wry neck. Mention may be made of the traumatic theory of Stromeyer,[1] in 1838. He thought that the condition resulted from tearing of the sternocleidomastoid muscle during difficult labor, with resulting hematoma formation, fibrous repair and shortening of the muscle. Petersen,[2] in 1884, ascribed intra-uterine shortening of the muscle to an early adherence of the skin of the healthy side of the face to the amnion. Mikulicz and Kader,[3] in 1895, considered wry neck to be the consequence of a chronic progressive myositis that occurred through an intrapartum, hematogenous infection. Völcker,[4] in 1902, stressed the idea that torticollis resulted from an ischemic muscular contracture in intra-uterine life, through pressure of the shoulder on the chief artery of the sternocleidomastoid. The most plausible hypothesis is that the cause of most of the congenital cases of muscular wry

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Read before the Chicago Pediatric Society, Dec. 16, 1930.

1. Stromeyer, G. F.: Beiträge zur operativen Orthopädik, oder Erfahrungen über die subcutane Durchschneidung verkürzter Muskeln und deren Sehnen, Hannover, Helwing, 1838.

2. Petersen, F.: Caput obstipum, Arch. f. klin. Chir. **30**:4 and 781, 1884; Zur Frage des Kopfnickerhämatoms bei Neugeborenen, Zentralbl. f. Gynäk. **10**:777, 1886; Zentralbl. f. orthop. Chir. **1**:5, 1886.

3. Mikulicz, J.: Ueber die Extirpation des Kopfnickers beim muskulären Schiefhals, nebst Bemerkungen zur Pathologie dieses Leidens, Zentralbl. f. Chir. **22**:1, 1895. Kader, B.: Das Caput obstipum musculare, Beitr. z. klin. Chir. **17**: 207, 1896-1897; **18**:173, 1897; Mitt. a. d. Grenzgeb. d. Med. u. Chir. **2**:731, 1897.

4. Völcker, F.: Das Caput obstipum; eine intrauterine Belastungsdeformität, Beitr. z. klin. Chir. **33**:1, 1902.

neck is a pathologic condition originating *in utero*. Less commonly, anomalous vertebrae and cervical ribs may cause a decided tilting of the head.

The acquired forms of muscular torticollis of short duration most frequently follow infectious processes that arise from the nasopharynx, tonsils or lymph nodes, and produce general muscular involvement, with pain, tenderness, local edema and evidence of sepsis. Tuberculosis of the cervical spine commonly produces wry neck. Early in its course it may be difficult to recognize, but the characteristic clinical course of tuberculosis, the various reactions to tuberculin and the later roentgenographic picture of caries of the spine make the diagnosis apparent. Infrequent causes are cervical dislocation, fracture and osteo-arthritis. Spasmodic torticollis, involving the spinal accessory and upper cervical nerves in their distribution to the cervical muscles, has been variously explained, and is seldom seen in childhood. Tics and psychoneuroses are also rarely encountered. The eleventh nerve may be involved anywhere in its course with resulting paralysis of the sternocleidomastoid and a portion of the trapezius. Torticollis is then present with inclination of the head toward the sound side.

Tilting of the head may result from an entirely different set of factors than those mentioned. The literature contains numerous reports of torticollis secondary to paralysis of the ocular muscles, anomalies of refraction, changes in the labyrinth, tumors of the cerebellum and hemorrhage into the central ganglions. A surprisingly large number of infants show a small degree of head tilting. This is apparently due to ocular muscle imbalance, which disappears by the second year of life. In not a small number the tilting persists. In contrast to muscular torticollis and that due to fixed changes in the cervical spine, ocular torticollis permits of free voluntary movement of the head in all directions long after the onset of the condition. It is to this type of case, with head tilting secondary to disturbances of the eyes, that I wish to direct particular attention. The mechanism of the production of the abnormal position of the head is of special interest.

ANATOMY AND PHYSIOLOGY OF THE EXTRA-OCULAR MUSCLES

Normal binocular single vision is largely the result of coordination of the extra-ocular muscles, the two obliques and the four recti. Certain phases of the anatomy and physiology of these muscles will be briefly reviewed. The action of the internal and external recti is simple and obvious; that of all the other muscles is more complex, being made up of two or three components. The nature of the origin of the superior and inferior recti from the nasal or medial side of the orbit at the annulus tendineus communis and their insertion laterally into the anterior half of the eyeball (in front of the equator) causes these

muscles to be subsidiary adductors, and also primary elevators and depressors, respectively. Examination of figure 1, *A* and *B*, will make this apparent.

The superior oblique arises from the sphenoid at the optic foramen, runs forward along the medial wall of the orbit to the trochlea, a fibrous pulley, and then turns back at an angle of 50 degrees, to be inserted behind the equator of the eyeball. The inferior oblique arises from the medial wall of the orbit (superior maxilla) and is also inserted behind

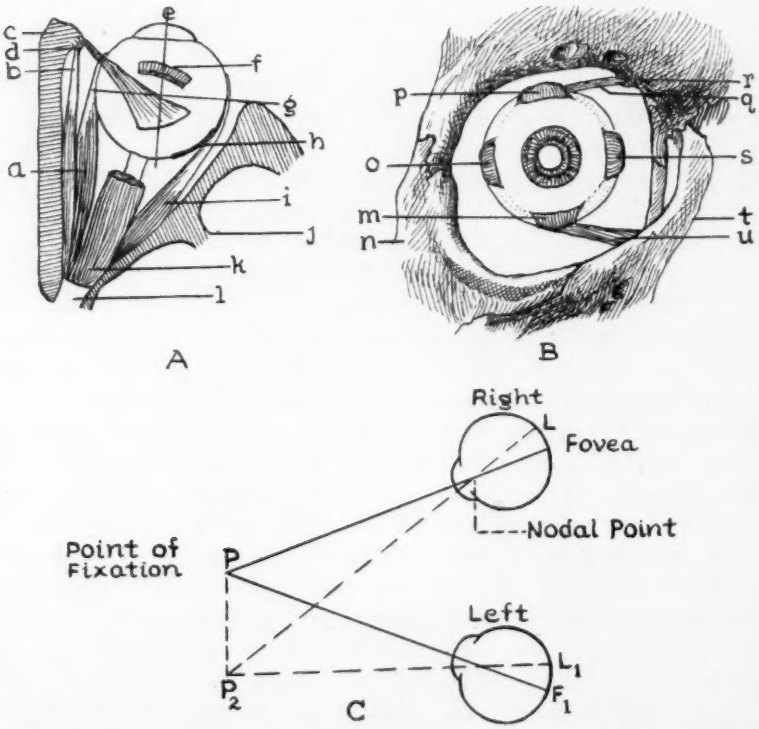

Fig. 1.—*A* represents the orbit from above (schematic view, according to Fuchs [Fuchs, Ernst: Text-Book of Ophthalmology, authorized translation from the twelfth German edition by Alexander Duane, ed. 5, Philadelphia, J. B. Lippincott Company, 1917, p. 713]): *a*, internal rectus; *b*, superior oblique; *c*, internal wall of the orbit; *d*, trochlea; *e*, sagittal axis of the eyeball; *f*, insertion of superior rectus; *g*, equator of the eyeball; *h*, line of insertion of inferior oblique; *i*, external rectus; *j*, external wall of the orbit; *k*, superior rectus (cut off), and *l*, foramen opticum. *B* shows an anterior view of the orbit (schematic view, according to Fuchs): *m*, insertion of inferior rectus; *n*, zygoma; *o*, external rectus; *p*, insertion of superior rectus; *q*, tendon superior oblique; *r*, trochlea; *s*, internal rectus; *t*, superior maxilla, and *u*, inferior oblique. *C* indicates binocular single vision (P_2, situated to the left of the point of fixation, causes image at *L* and L_1, equidistant from and to the right of the fovea in both eyes).

the equator. Because of their insertions, their action is obviously that of subsidiary abduction, the superior oblique being primarily a depressor and the inferior oblique an elevator. With the exception of the internal and external recti, all the other extra-ocular muscles have in addition a torsion action, which moves the eyeball nasalward or templeward.

The superior oblique is innervated by the fourth cranial nerve (trochlearis), the external rectus by the sixth or abducens nerve, and the remaining muscles by the third or oculomotor nerve.

In the act of normal vision one unconsciously adjusts the eyes so that the image of an object is focused on the fovea of each eye. In

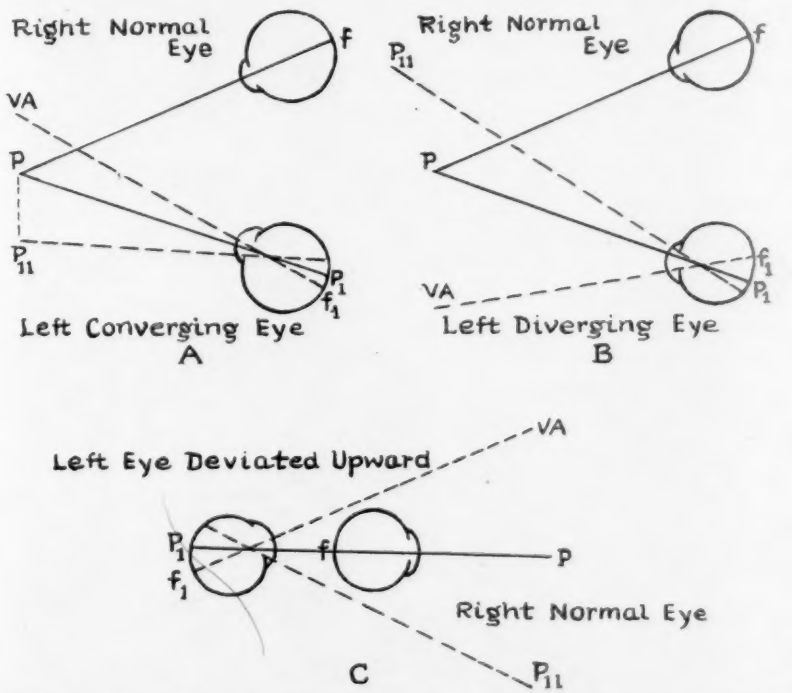

Fig. 2.—*A* indicates homonymous diplopia; *B*, crossed diplopia, and *C*, vertical diplopia.

other words, the image passes along an imaginary straight line from the object through the nodal point to the retina; and when symmetrical points on the retina of each eye are stimulated, a fusion occurs in the brain, which gives the mental concept of a single image, or binocular single vision. Further, experience teaches one to orient objects in space (projection of images), in that objects situated to the right of the center of fixation produce images to the left of the fovea, and vice versa. Likewise, objects above or below the point of fixation throw their images below or above the fovea, respectively (fig. 1, *C*).

DIPLOPIA

When the visual axis of one eye deviates, there is a loss of binocular single vision, and binocular diplopia occurs. The manner in which this takes place may be explained simply (fig. 2, *A*). Suppose the right eye to be normal and the left eye to be convergent. The normal visual axis, *Pf*, of the right eye enables the point of fixation, *P*, to cast its image exactly on the fovea, *f*, while the visual axis *VA*, of the left eye is deviated inward, so that the point of fixation, *P*, casts its image, P_1, to the right of the fovea, f_1, of the left eye, and hence is projected to the left at P_{11}. In this example, the person, being unconscious of the inward deviation of the left eye, expects the object to throw its image on the fovea, whereas the image falls to the right; hence he makes the subjective mistake of thinking that the object has become displaced to the left, and double images result. This is an example of what is termed homonymous diplopia, since the false image of the paralyzed eye is projected on the same side. This is seen in convergent strabismus, resulting from paralysis of an abductor muscle (external rectus, superior and inferior oblique).

When an eye deviates outward, there results crossed diplopia. If the right eye is normal and the left diverges, the point of fixation, *P*, is seen normally at the right fovea, *f*, whereas in the left eye it casts its image to the left of the fovea, f_1, and hence is projected to the right at P_{11}, and the image of the left eye is to the right of that of the right eye, i. e., crosses it, and crossed diplopia results (fig. 2, *B*). This characterizes divergent strabismus, resulting from paralysis of an adductor muscle (internal, superior and inferior rectus).

A difference in the level of double images or vertical diplopia may also be explained simply (fig. 2, *C*). If the right eye is normal and the left deviates upward, the point of fixation, *P*, is seen normally at the fovea, *f*, of the right eye, while in the left eye the image falls above its fovea, f_1, and hence is projected below at P_{11}, and the images are at different levels, the lower image belonging to the eye that is deviated upward, as in paralysis of a depressor muscle (superior oblique and inferior rectus). When the eye deviates downward, its image is the higher one, as in paralysis of an elevator muscle (inferior oblique and superior rectus).

Inclination of double images proceeds according to the same rules; hence the image of the paralyzed eye (termed the false image) is always inclined in a direction opposite to that in which the eye is deviated.

PARALYSIS OF OCULAR MUSCLES AND HEAD TILTING

Of the etiologic factors involved in the production of paralysis of the ocular muscles mention may be made of the following: congenital

anomalies of the ocular motor nuclei; acquired paralysis resulting from diphtheria, anterior poliomyelitis, epidemic encephalitis, syphilis and other infectious and toxic conditions; fracture of the skull and involvement especially of the fourth and sixth cranial nerves.

One or more muscles may be affected at the same time. The superior oblique and the external rectus are most frequently involved. This is due to the long course of the fourth and sixth nerves, which renders them prone to injury. Paralysis of the superior and inferior rectus is less frequent. Various combinations also occur.

The diagnosis of paralysis of an affected muscle is dependent usually on three factors: limitation of movement of the affected eyeball, deviation of the eye and diplopia. The exact diagnostic procedure belongs in the field of ophthalmology. Head tilting or torticollis is the compensatory adjustment of the head to overcome vertical diplopia. Ordinary normal ocular excursions are from 20 to 30 degrees. Beyond this, the head rotates.

A simple experiment that offers a practical demonstration of the mechanism of production of torticollis in diplopia may be carried out if, with the eyes fixed on a nearby object, one makes pressure in a vertical direction on one eyeball. This is to simulate the abnormal rotation of the eyeball that occurs in paralysis of an extra-ocular muscle concerned with vertical movement. Artificial diplopia results, the false image belonging to the eye against which the force is directed. With the finger maintaining constant pressure, it will be found that the head must be tilted in one direction or the other in order to produce a fusion of the two images with a disappearance of the diplopia. This is artificial ocular torticollis. However, it must be borne in mind that the conditions in the experiment are not at all like those in paralysis of an extra-ocular muscle, because in the experiment there is involuntary ocular accommodation.

Duane [5] stated that "the image belonging to the paralyzed eye is displaced in just that direction in which the affected muscle, if intact, would naturally move the eye. This rule shows us that in paralysis of the subsidiary adductors (superior rectus and inferior rectus) we expect to find a crossed diplopia and in paralysis of the subsidiary abductors (the two obliques) we shall find an homonymous diplopia."

In table 1 are noted the phenomena occurring in paralysis of the extra-ocular muscles, in consequence of which there are vertical diplopia and torticollis.

Diplopia occurs when the gaze is directed in the normal field of action of the paralyzed muscle, and likewise, displacement of the false image of the paralyzed eye is in the same plane. Hence, as previously

5. Duane, A., in Fuchs, H. E.: Textbook of Ophthalmology, ed. 6, Philadelphia, J. B. Lippincott Company, 1919, p. 750.

stated, in paralysis of the elevators (superior rectus and inferior oblique), the false image is the higher, while in paralysis of the depressors (inferior rectus and superior oblique) the false image is the lower. The head is always tilted to the side of the higher image, whether it belongs to the normal or to the paralyzed eye. This is an attempt on the part of the patient to correct the vertical diplopia by bringing the images to the same level.

When the right superior rectus is paralyzed, its image is the higher on the left side (crossed adductor diplopia) and the head is tilted to the left side. Paralysis of the right inferior oblique causes the higher image to be on the right side (homonymous diplopia) and the head is inclined to the right. Since the image of the depressors is the lower,

TABLE 1.—*Ocular Torticollis*

	Muscle	Normally Moves Eyeball	Paralyzed Eye Deviates	False Image	Diplopia	Head Tilted to		Face Directed	
						Right Eye	Left Eye	Right Eye	Left Eye
Elevators									
Adductor	Superior rectus	Upward and inward	Downward and outward	Higher	Crossed	Left shoulder	Right shoulder	Upward and to left	Upward and to right
Abductor	Inferior oblique	Upward and outward	Downward and inward	Higher	Homonymous	Right shoulder	Left shoulder	Upward and to right	Upward and to left
Depressors									
Adductor	Inferior rectus	Downward and inward	Upward and outward	Lower	Crossed	Right shoulder	Left shoulder	Downward and to left	Downward and to right
Abductor	Superior oblique	Downward and outward	Upward and inward	Lower	Homonymous	Left shoulder	Right shoulder	Downward and to left	Downward and to right

the head is turned to the opposite side (that of the higher image), so that in paralysis of the right inferior rectus (crossed diplopia) the head is tilted to the right shoulder, and in involvement of the right superior oblique (homonymous diplopia) the head is inclined to the left. When the head is in the abnormal compensating position, diplopia disappears; when the head is erect, diplopia is present.

Vertical diplopia and torticollis do not occur with involvement of the adducting internal rectus or abducting external rectus. The sphere of action of these muscles is purely horizontal, so that the head is rotated to the right side in paralysis of a right rotator and to the left side in paralysis of a left rotator. Even as the tilting of the head in vertical diplopia is a compensatory mechanism, so the deflection of the face is to compensate for the other components, such as rotation and torsion or deflection of the vertical meridian. In paralysis of the elevators (superior rectus and inferior oblique) the face is directed upward, and in paralysis of a depressor (inferior rectus and

superior oblique) the face is directed downward. For the sake of simplicity, these subsidiary actions will not be discussed further.

SPASM OF EXTRA-OCULAR MUSCLES

There is another phase of this problem that can be readily appreciated. Spasm of an associate muscle (superior oblique and inferior rectus, inferior oblique and superior rectus, internal and external rectus) may produce a condition that corresponds to the paralysis of its fellow, and further, diplopia increases as the gaze is directed in the field of action of the overacting muscle. Spasm is occasionally seen secondary to meningitis, disorders of the brain, disturbances of the labyrinth and tetanus. It is common as the secondary spasmodic deviation of the sound eye when the paralyzed eye fixes (Duane[6]). The conditions are as shown in table 2.

TABLE 2.—*Spasm of the Ocular Muscles (After Fuchs[6])*

		In Either Case			
Spasm of Right*	Corresponds to Paralysis of Left*	If Left Eye Fixes, Right Deviates Greatly	If Right Eye Fixes, Left Deviates Somewhat	Diplopia (Vertical)	Head Tilted to
Superior rectus	Inferior oblique	Upward	Downward	Image of right eye is below	Left shoulder
Inferior oblique	Superior rectus	Upward	Downward	Image of right eye is below	Right shoulder
Inferior rectus	Superior oblique	Downward	Upward	Image of left eye is below	Right shoulder
Superior oblique	Inferior rectus	Downward	Upward	Image of left eye is below	Left shoulder

* The conditions obtaining in spasm of the left eye (paralysis of the right) may be deduced by substituting right for left, and vice versa.

LITERATURE AND CASE REPORTS

Historically, Cuignet,[7] in 1873, first used the term "ocular torticollis," when he called attention to tilting of the head of the type resulting from inequality in the oculomuscular balance. However, as early as 1864, Graefe[8] taught that compensation for paralysis of the superior oblique muscle could be accomplished by a tenotomy of the inferior rectus muscle of the sound eye. Knapp,[9] in 1874, Kries,[10] in 1878, and

6. Duane,[5] p. 759.

7. Cuignet: Rec. d'opht. **1**:338, 1873.

8. von Graefe, A.: Aphorismen über Tenotomie insonderheit gegen paralytische Diplopia, Klin. Monatsbl. f. Augenh. **1**:1, 1864.

9. Knapp, H.: Tenotomie des oberen oder unteren geraden Augenmuskels, Arch. f. Augenh. **4**:92, 1874.

10. Kries, N. V.: Operative Heilung dreier Fälle von Trochlearislähmung, Arch. f. Ophth. **24**:148, 1878.

Landolt,[11] in 1885, published further observations on the operative possibilities in paralysis of the trochlear nerve. Graefe [12] presented twenty cases in 1887. Landolt,[13] in 1890, reviewed the entire subject of ocular torticollis, and also quoted the reports of Wadsworth,[14] Risley,[15] Morosow,[16] Nieden,[17] Lovett [18] and Bradford.[19]

In 1902, Posey,[20] studying the associated movements of the head and eyes, concluded that the vicarious position of the head was assumed to compensate for some imperfect action of one or more of the extraocular muscles.

Pick,[21] in 1907, showed a boy of 11 years with a right torticollis present since the age of 1 year, following diphtheria. For three years he was treated by orthopedists without success. Examination showed no sternomastoid shortening. On the contrary, there was paralysis of the left superior oblique muscle, with the appearance of double images when the abnormal position of the head was corrected. By tenotomy of the right inferior rectus muscle, the inclination of the head was considerably improved.

Stephenson,[22] in 1912, reported the case of a girl who showed a right torticollis. With the head in the abnormal position, the right eye was free from squint, but at other times inclined downward from 8 to 10 degrees. With the head straight, the right eye would squint downward or the left upward. When the head was tilted, there was no diplopia; when it was held straight, double images were seen.

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11. Landolt, E.: La tenotomie de l'oblique inférieur, Arch. d'opht. **5**:402, 1885.

12. von Graefe, A.: Die Indicationsstellung bei operativer Behandlung der paralytisch bedingten Deviationen eines Auges, Arch. f. Ophth. **33**:179, 1887.

13. Landolt, E.: Torticollis oculaire, Bull. méd., Paris **4**:573, 1890.

14. Wadsworth, O. F.: Spastic Torticollis, Apparently Due to Faulty Position of the Eyes, and Cured by Tenotomy, Tr. Am. Ophth. Soc., 1889, p. 381.

15. Risley, S. D., quoted by Landolt, E., in Norris, W. F., and Oliver, C. A.: System of Diseases of the Eyes, Philadelphia, J. B. Lippincott Company, 1900, vol. 4, p. 74.

16. Morosow, quoted by Landolt, E., in Norris, W. F., and Oliver, C. A.: System of Diseases of the Eyes, Philadelphia, J. B. Lippincott Company, 1900, vol. 4; Vrach **11**:743, 1890.

17. Nieden: Ein Fall von functionellen Torticollis bedingt durch eine Augenmuskellähmung, Centralbl. f. prakt. Augenh. **16**:321 (Nov.) 1892.

18. Lovett, R. W.: A Case of Functional Torticollis, Probably Due to Defective Eyesight, Tr. Am. Orthop. A. **2**:230, 1889.

19. Bradford, E.: Case of Functional Torticollis from Defective Eyesight, Tr. Am. Orthop. A. **1**:48, 1889; Centralbl. f. orthop. Chir. **9**:85, 1890.

20. Posey, W. C.: Associated Movements of Head and Eyes, J. A. M. A. **39**: 1365 (Nov. 29) 1902.

21. Pick, L.: Schiefhals, Deutsche med. Wchnschr. **33**:1617, 1907.

22. Stephenson: Ocular Torticollis, Proc. Roy. Soc. Med. (Sect. Ophth.) **6**:90 (Nov.) 1912; Ophthalmoscope **7**:113, 1909.

Pierola,[23] in 1914, detailed a case of ocular torticollis and left vertical strabismus of 15 degrees in a youth aged 17; the strabismus was present at birth, and torticollis at the age of 1½ months. The head was over the right shoulder, and the right side of the face was badly developed. The abnormal position gave normal binocular vision. Cure was accomplished by advancement of the left inferior rectus.

Cockayne's [24] patient (1914) was a boy of 6½ years, in whom left torticollis developed at the age of 2 months. Orthopedic appliances were used with failure. There was a compensatory spinal curvature of the cervicodorsal region with the convexity to the right. Facial asymmetry was present. There was no squint in the position naturally assumed, but when the head was straightened the right eye deviated upward and inward. There was no astigmatism. Diplopia was probably present, and the ocular movements were good. There was no shortening or rigidity of the sternomastoid.

In 1916, Duane [25] presented the classical case of a girl 6 years and 9 months of age. Massage and orthopedic appliances used since the age of 6 months, were without result. At the age of 2, when the head was straightened by means of a brace, it was noticed that the left eye deviated upward. The mother, suspecting that the eyes had something to do with the difficulty, tried the effect of bandaging the left eye. The child at once held the head straight. Duane's examination showed the head to be tilted markedly to the right shoulder and turned somewhat to the right. When the head was in this position, the screen test (alternate covering) showed a left hyperphoria of about 10 degrees. When the head was held straight, this hyperphoria increased to more than 20 degrees. There was hardly any lateral deviation in the associated movements upward and to the right. With the right eye fixing, the left eye would shoot high up, and the same would happen when the eyes were directed far to the right on the horizontal plane. In other directions of the gaze, and particularly in the lower field both to the right and to the left, there was little deviation and the movements of the eyes were concomitant. The diagnosis was: "congenital insufficiency of the right superior rectus; fixation with this paretic eye; sharp secondary deviation upward of the left sound eye. Tilting of the head in order to bring vertically displaced images more on a level."

Krückman,[26] in 1924, effected a cure in ocular torticollis due to paralysis of the superior oblique by recession of the inferior rectus of the sound eye.

23. Pierola: Ocular Torticollis, Arch. d'opht. **33**:754, 1914.

24. Cockayne, E. A.: Case of Ocular Torticollis, Proc. Roy. Soc. Med. (Sect. Dis. Child.) **7**:99, 1914.

25. Duane, A.: Torticollis Relieved by Tenotomy of the Inferior Oblique, Arch. Ophth. **45**:1 (Jan.) 1916.

26. Krückman: Ocular Torticollis, Klin. Monatsbl. f. Augenh. **72**:538, 1924.

Heuser,[27] in 1924, reported three cases of congenital torticollis, all with typical paralysis of the superior oblique muscle. One child of 7 years was successfully operated on by tenotomy of the inferior rectus of the opposite eye. All the children showed asymmetry of the face, but no abnormality of the spinal column.

In addition to the previous reports, there have been many excellent contributions by Isakowitz,[28] Bielschowsky,[29] White,[30] Kremer,[31] Van Lint,[32] Stewens,[33] Rey and Hentschel,[34] Elschnig [35] Arganaraz [36] Braun [37] and others.

REPORT OF CASES

CASE 1.—A boy of 4½ years was referred by Dr. M. L. Blatt to the pediatric clinic at the University of Illinois on Nov. 5, 1925. The mother stated that the child had maintained his head to the right shoulder since he was 3 months old and was "cross-eyed." Several attempts had been made to correct the malposition of the head by means of plaster of paris casts, collars and massage, but the treatment had been unsuccessful. Examination showed that voluntary rotation of the cervical spine was normal, the child being able to bend his head to touch the right or left shoulder. The sensory, cranial and peripheral reflexes were normal. There was no contracture or spasticity of the right sternocleidomastoid muscle. Roentgenograms of the cervical and upper thoracic portions of the spine disclosed small cervical ribs in connection with the sixth and seventh cervical vertebrae, especially

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27. Heuser: Congenital Torticollis, Ztschr. f. Augenh. **53**:114, 1924.

28. Isakowitz, J.: Torticollis from Congenital Trochlearis Paralysis, Centralbl. f. prakt. Augenh. **37**:168, 1913.

29. Bielschowsky, A.: (*a*) in Graefe-Saemisch: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, Wilhelm Engelmann, 1907. (*b*) Beitrag zur operativen Behandlung der Vertikalablenkung der Augen, Arch. f. Ophth. **105**:656, 1921; (*c*) Ueber die operative Behandlung veralteter Trochlearis-Paresen, Klin. Monatsbl. f. Augenh. **69**:611, 1922; (*d*) Abnorme Kopfhaltung infolge von Augenmuskelstörungen, Deutsche med. Wchnschr. **49**:1387, 1923; (*e*) Indikationen und Resultate der Myektomie des Obliquus inferior, Ztschr. f. Augenh. **58**:57, 1925; (*f*) Torticollis infolge angeborener Ueberfunktion des Obliquus inferior dexter, Klin. Monatsbl. f. Augenh. **80**:394, 1928.

30. White, J. W.: Tenotomy of the Inferior Oblique, New York State J. Med. **20**:156, 1920.

31. Kremer: Ueber die operative Behandlung veralteter Trochlearis-Paresen, Klin. Monatsbl. f. Augenh. **69**:600, 1922.

32. van Lint: Ocular Torticollis of Unknown Origin, Bull. Soc. belge d'opht. **49**:12, 1924.

33. Stewens, H.: Angeborene Beweglichkeitsstörungen der Augenmuskeln, Ztschr. f. Augenh. **65**:1, 1928.

34. Rey, E. J., and Hentschel, F.: Functional Torticollis and Visual Disturbances, Ztschr. f. orthop. Chir. **50**:371 (Oct. 19) 1928.

35. Elschnig: Torticollis. Eye Changes, Verhandl. d. deutsch. orthop. Gesellsch. (1928), Kong. 23, 1929, p. 168.

36. Arganaraz, R.: Paralytic and Functional Vertical Strabismus and Torticollis, Semana méd. **2**:737 (Sept. 12) 1929.

37. Braun, G.: Etiology and Close Relationship of Ocular and Surgical Torticollis, Med. Klin. **25**:590 (April 12) 1929.

marked on the left side. Prior to ophthalmologic examination this was confusing. The findings in the eyes were: The left eye turned upward on looking straight ahead, this being more marked under cover. Abduction and adduction appeared normal. Refraction disclosed right compound hyperopic astigmatism and left hyperopia. The muscle imbalance was diagnosed as a congenital insufficiency of the right superior rectus. Glasses were fitted, but produced no improvement. Operation was advised but was refused.

Case 2.—Study of a girl of 7 years at the University of Illinois pediatric department on Feb. 14, 1925, suggested the diagnosis of cerebral infantile paralysis of a mild character. The head was held inclined to the right shoulder, and the left eye was turned upward and inward when the head was straightened. Examination of the eyes disclosed a compound hyperopic astigmatism and a concomitant alternating squint. The tendency of the left eye to shoot upward and inward was interpreted as significant of a paralysis of a left depressor muscle, and the final diagnosis was insufficiency of the left superior oblique. Consent for operation could not be obtained.

Case 3.—In a boy of 8 years a right torticollis had developed at the age of 8 months, following a fever of unknown origin. At examination the right eye was deviated downward and inward, and could not be moved upward and outward. On looking upward, the right eye turned upward and inward. There was also bilateral, compound hyperopic astigmatism. The muscle imbalance was diagnosed as paralysis of the right inferior oblique and spasm of the right superior rectus. The wearing of corrective glasses decreased the extent of tilting of the head.

Head tilting may result from another set of factors. There are many instances of a fairly common condition in which the patient tilts the head so as to eliminate the influence of an oblique meridian astigmatism.

Lewis,[38] in 1903, published the case of a girl, aged 8 years, with a marked right torticollis. Attention to test letters caused rhythmic swaying of the head from side to side, and study showed this to be her habit of scrutiny, at least for distant observation. Examination of the eyes disclosed hyperopic astigmatism, no lack of binocular single vision and no nystagmus.

Dimmer,[39] in 1907, cited the case of a patient who could read only when letters were vertical, and who held his head in an abnormal position to accomplish this.

Bankart and Dawnay,[40] in 1923, reported wry neck on the left side in a boy of 7 years. There were no contractures, and the deformity could be voluntarily corrected. The left eye was found to be amblyopic,

38. Lewis, E. R.: Report of a Case of Pseudo-Torticollis with Abnormal Associated Movements of Head and Eyes, Ophth. Rec. **12**:22 (Jan.) 1903.

39. Dimmer, F.: Lesen bei vertikaler Stellung der Zeilen, Arch. f. Ophth. **66**: 189, 1907.

40. Bankart and Dawnay: Torticollis of Ocular Origin, Proc. Roy. Soc. Med. (Sect. Dis. Child.) **6**:18, 1913; in Jackson, E.: Ophthalmic Year Book, Chicago, Ophthalmic Publishing Company, 1913, vol. 10, p. 100.

and refraction showed oblique hypermetropic astigmatism in both eyes but greater in the left.

White,[41] in 1928, and Braun,[37] in 1929, emphasized the importance of uncorrected high degrees of astigmatism in the production of head tilting.

Marbaix,[42] in 1921, observed deviations of the head in astigmatism, ocular palsies or insufficiencies following tenotomy, ptosis, severe diseases of the brain and nystagmus, and cited six illustrative cases.

CASE 4.—A malnourished girl of 12 years was presented for advice concerning dorsal kyphosis and tilting of the head to the right. The condition had been present for eight years. At one time the child was in a body cast for eight months. There was no complaint of diplopia. The head could be voluntarily moved in all directions. Ophthalmologic examination by Dr. J. E. Lebensohn revealed normal muscle balance, but marked myopic astigmatism, especially in the right eye. With correction of the ocular refractive error, and the institution of proper hygienic and dietetic treatment and graduated postural exercises, after two years the head was held straight and the spinal curvature was much improved.

Ocular or congenital nystagmus, with its even pendulum-like movements of varying velocity (in contrast to labyrinthine nystagmus), may produce tilting of the head. Fuchs [43] stated that nystagmus is caused by conditions producing bilateral amblyopia in early infancy, such as opacities of the cornea, especially from ophthalmia neonatorum, congenital cataract, disease of the retina and choroid, total congenital color blindness and albinism. The condition may disappear during childhood.

Braun,[37] in 1929, quoted the report of Budek [44] (1913), who described two instances of nystagmus during reading, overcome by abnormal position of the head.

White,[41] in 1928, mentioned head tilting due to nystagmus, in which condition the head is turned so as to put the eyes in the field of the slower component.

CASE 5.—A girl of 10 years had a marked optic nystagmus at birth. The head was in constant motion from side to side, and this was exaggerated after the child was able to sit up. The head was tilted to one or the other shoulder and was never held erect. At the age of 2 years she had a short spell of severe pharyngitis with hyperpyrexia, following which the nystagmus abruptly disappeared, and with it the movements and tilting of the head. Her vision at the time of this report is entirely normal.

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41. White, J. W.: Head Tilting and Turning of Ocular Origin, Am. J. Surg. **4**:77 (Jan.) 1928.

42. Marbaix: Deviations of the Head in Ophthalmology, Am. J. Ophth. **4**:282, 1921.

43. Fuchs, H. E.: Textbook of Ophthalmology, ed. 6, Philadelphia, J. B. Lippincott Company, 1919, p. 799.

44. Budek, R.: Ueber Lesen bei vertikaler Stellung der Zeilen, Med. Klin. **36**:1454, 1913.

CASE 6.—A female mongolian idiot aged 18 months had had nystagmus since birth. The head was inclined to the right shoulder at all times; there was no apparent muscle imbalance, and the eyes followed objects well. This is an example of head tilting associated with nystagmus of unknown origin.

COMMENT AND TREATMENT

Ocular torticollis is emphasized because of its importance in pediatric medicine. Recognition of the possible relationship of torticollis to ocular defects will spare children unnecessary operations, prolonged immobilization by collars and casts and other orthopedic measures. Correction of the ocular defect is at the same time the cure of the torticollis. When ocular torticollis is allowed to go uncorrected, or rather when the disturbance of the eye is not remedied, the patient ultimately learns to ignore the image of the paralyzed eye, and binocular single vision is lost, uni-ocular vision remaining, with amblyopia of the involved eye. Prolonged tilting of the head finally results in changes in the cervical musculature and spine, and asymmetry of the face and even of the skull (Rey and Hentschell [34]).

Treatment should be carried out by a competent ophthalmologist. As stated earlier, the usual procedure is to produce a defect in motility in the sound eye which is similar to the defect in the paralyzed eye, so that equilibrium may be restored in both eyes. This is effected by a backward insertion of the associate muscle of the sound eye, (in paralysis of the superior oblique, operation on the inferior rectus of the non-paralyzed eye). This procedure results in the corresponding meridians of the retinae of the eyes becoming parallel again, with disappearance of vertical diplopia (Bielschowsky [29d]). Proper refraction is also essential.

Finally, orthopedic measures and corrective exercises should be employed, when it is deemed necessary, following treatment of the eyes.

5430 West Adams Street.

Case Reports

NEUROFIBROMATOSIS OF THE BLADDER

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Von Recklinghausen's disease, multiple neurofibromatosis, is characterized by the formation of multiple connective tissue tumors on the nerve trunks, especially on the small cutaneous nerves.[1] Pigmentation of the skin is almost constantly present in well developed cases. The first tumors to appear are usually those on the cutaneous nerves. Later tumors may develop on the larger and more deeply situated nerves. Tumors often develop on the intracranial portions of the cranial nerves and on the roots of the spinal nerves, giving rise to symptoms of tumor of the brain and tumor of the cord, respectively. Tumors developing on the sympathetic nerve trunks have been reported, but apparently they are rare in this situation.

The disease is frequently congenital, but the earliest manifestations may first appear in early childhood or at puberty. More frequently, the first symptoms develop in adult life. The condition occurs in successive generations, and appears to be a dominant factor in inheritance.[2] The progress of the disease is often affected by metabolic disorders.[3]

Apparently, neurofibromatosis of the bladder in children has not been recorded in the literature. In a total of one hundred and twenty cases of von Recklinghausen's disease seen at the Mayo Clinic, one occurred in a child 13 years of age. The only instance of involvement of the urinary system in this series occurred in a man, aged 60, with a cord bladder resulting from tumors of the second and third sacral nerves.[4] In the intestinal form, the tumors may occur at any point from the lips to the anus.[5] Sarazanes collected cases in which the entire

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From the Department of Pathology, University of Minnesota, and the Minneapolis General Hospital. Reported with permission of Dr. E. J. Huenekens.

1. Bell, E. T.: A Textbook of Pathology, Philadelphia, Lea & Febiger, 1930, p. 187.
2. Prieser, S., and Davenport, C.: Multiple Neurofibromatosis and Its Inheritance, Am. J. M. Sc. **156**:507, 1918.
3. Penfield, W., and Young, A. W.: The Nature of von Recklinghausen's Disease and the Tumors Associated with It, Arch. Neurol. & Psychiat. **23**:320 (Feb.) 1930.
4. Braasch, W. F.: Personal communication.
5. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1928, p. 170.

gastro-intestinal tract and bladder showed multiple neurofibromatosis.[6] Lehman reported the case of a woman, aged 30, who had extensive tumors of the innominate bone, causing pressure on the bladder.[7] The tumors were neurofibromas that arose from a nerve in the periosteum. Winstine described an extensive case of von Recklinghausen's disease in a man 60 years of age.[8] Autopsy showed neurofibromatosis of the entire pelvic sympathetic plexus, especially around the bladder, rectum and vas deferens. The wall of the bladder was not involved by the tumors.

Neurofibromatosis of the bladder has been reported by Gerhardt (1878),[9] Kryieslies (1885),[10] Steden (1923),[11] Heusch (1926)[12] and Heidler (1928).[13] All of these cases were observed in adults.

Gerhardt's patient, a man 30 years of age, showed a marked generalized neurofibromatosis with compression of the spinal cord by intraspinal tumors. There were numerous neurofibromas within the thoracic and abdominal cavities, involving the sympathetic nerves, the mesentery and the viscera. There were many small tumors on the neck of the bladder. Kryieslies gives the autopsy report of an adult dying with neurofibromatosis, who showed many pea-sized nodules on the surface of the bladder. Steden reported a case of von Recklinghausen's disease of the bladder in a woman 31 years of age whose complaints were pain in the lower left abdominal quadrant, urinary difficulties and marked constipation. In addition to the subcutaneous nodules and pigmentary changes in the skin, the patient presented a large abdominal tumor above the symphysis pubis. Laparotomy and subsequent biopsy of a nodule removed from the surface of the bladder revealed multiple

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6. Sarazanes, G., cited by Ewing: Thèse, Paris, 1904.

7. Lehman, E. P.: Recklinghausen's Neurofibromatosis and the Skeleton, Arch. Dermat. & Syph. **14**:178 (Aug.) 1926.

8. Winstine, F.: The Relation of von Recklinghausen's Disease (Multiple Neurofibromatosis) to Giant Growth and Blastomatosis, J. Cancer Research **8**:409, 1924.

9. Gerhardt, C.: Zur Diagnostik multiples Neurombildung, Deutsches Arch. f. klin. Med. **21**:268, 1878.

10. Kryieslies, A., cited by Heusch: Ein Beitrag zu den multiplen Fibromen der Haut und den multiplen Neuromen, Inaug. Diss. zur Erlangung der Doktorwürde in der Medizin, Chirurgie und Gebürtshilfe, Göttingen, Dieterische Universitäts Buchdruckerei, W. F. Kaestner, 1885.

11. Steden, E.: Recklinghausen's Disease Involving the Bladder, Deutsche Ztschr. f. Chir. **177**:137, 1923.

12. Heusch, K.: Neurofibromata of the Bladder with Generalized Neurofibromatosis, Ztschr. f. urol. Chir. **21**:113, 1926.

13. Heidler, H.: Neurofibromata, Zentralbl. f. Gynäk. **52**:504, 1928.

neurofibromas. There were multiple nodules on the mucosa of the bladder over the trigone, which had obstructed the openings of the ureters and caused bilateral hydro-ureters and hydronephrosis.

The first diagnosis of neurofibromatosis of the bladder made during life was made by Heusch, with the aid of the cystoscope. His patient was a man 53 years of age with marked generalized neurofibromatosis, difficulty in voiding and pain on urination. Cystotomy was performed, and the small tumors previously observed through the cystoscope were removed. The nodules were situated in front of the neck of the bladder, and caused a definite urinary obstruction. Microscopic examination of the excised nodules confirmed the diagnosis of neurofibromatosis.

Heidler's patient was a woman 68 years of age with multiple neurofibromatosis of the skin and of the bladder. The patient had no urinary complaints. In view of the work of Heusch, a cystoscopic examination was made; it revealed many bean-sized nodules in the wall of the bladder. No microscopic examination of the tumors was made.

The uncommon occurrence of vesical involvement in neurofibromatosis and the infrequent occurrence of tumors of the bladder in children makes the following case of interest.

REPORT OF A CASE

History.—R. O., a white boy, aged 7 years, was admitted to the pediatric department of the Minneapolis General Hospital on July 16, 1931. About July 2, the patient had had an attack of hematuria which had lasted two days. He had had enuresis for three years, but had been practically free from this symptom during the present year. During the past three years he had been subject to recurrent attacks of severe headaches localized in the frontal region, and of irregular occurrence and duration. He had also complained of aching pains in the legs for the past year.

The parents stated that since birth the child had had a scattered small brown macular eruption of the skin and several beanlike subcutaneous nodules. They were first noted in the right cervical and posterior auricular regions and over the right shoulder. During the year before presentation, there had been a noticeable increase in the number of subcutaneous nodules and in the pigmentation of the skin. The nodules were now observed beneath the skin over the chest and trunk.

Birth had been normal. The child had pneumonia at 4 months and chickenpox at 5 years, and was subject to frequent infections of the upper respiratory tract. The mother was in good health; the father had hypertension. Two brothers were living and well; one brother died in infancy of intestinal obstruction. There was no familial history of any cutaneous disorders, and no history of tumors or pigmentary changes.

Physical Examination.—The patient was a well nourished, normally developed boy of average intelligence. The skin of the trunk showed numerous scattered, small, light brown macules that varied in shape and size, between 4 and 9 mm. in diameter. The pigmentation was most marked over the anterior and lateral aspects of the chest and abdomen. There were small beanlike subcutaneous nodules of fairly firm consistency. They were on the neck, arms and trunk. They

were freely movable and slightly tender. These nodules averaged 6 mm. in diameter and were slightly raised above the surface.

The tonsils were large and cryptic. There was moderate bilateral cervical adenopathy. The heart and lungs appeared normal. Examination of the abdomen revealed a large, firm, slightly tender mass in the suprapubic region, from 6 to 8 cm. in diameter, and extending upward about one third of the distance between the pubis and the umbilicus. The mass could be palpated rectally, and gave the impression of a tumor of the bladder or one involving the bladder and the rectum.

The clinical diagnosis was von Recklinghausen's disease with visceral involvement.

Course.—The patient was placed under observation for study of the genitourinary tract. One of the subcutaneous nodules was removed and proved to be

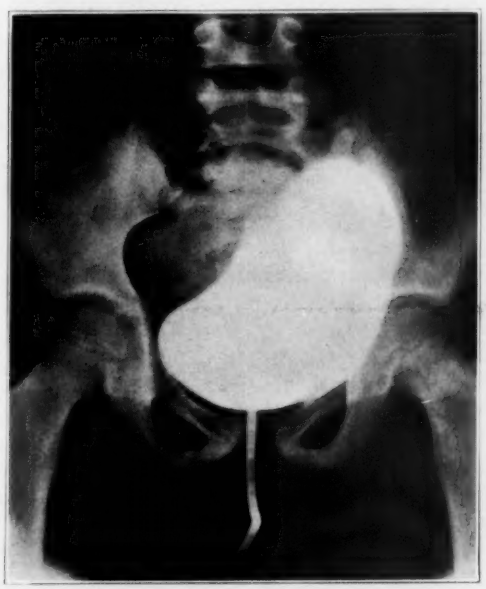

Fig. 1.—Roentgenogram of the bladder after filling with a 10 per cent solution of sodium iodide, demonstrating asymmetry due to involvement of the bladder by neurofibromas.

a neurofibroma. On August 4, the tonsils and adenoids were removed because of the repeated infections of the upper respiratory tract. Six hours following the operation, the patient's temperature rose to 104.5 F., rectally. He could not retain any fluid, and complained of marked soreness in his throat. Examination showed a moderate degree of thin, bloody gray exudate in the tonsillar fossae, not unlike that usually seen postoperatively. There was a marked redness of the posterior pharyngeal wall. The ears and chest showed no abnormalities. The blood pressure was 118 systolic and 80 diastolic. The patient's condition became progressively worse; the fever persisted, and he became delirious. On August 8, a typical scarlet fever eruption developed, and the patient was transferred to the contagious service. On August 11, bilateral suppurative otitis media developed. Following myringotomy, there was a profuse, thin, gray purulent discharge from

both ears. Later during the same day, acute arthritis of both wrist joints appeared. There were numerous moist râles throughout both lungs, with impaired resonance over the left base. The patient's condition continued to be critical; he appeared more toxic, and remained in a delirium. A solution of dextrose and fluids was given intravenously, and fluids were given subcutaneously.

Death occurred on August 13, apparently from bronchopneumonia and sepsis complicating scarlet fever.

Laboratory Data.—On July 16, studies made with iopax showed that the appearance of both renal pelves and both ureters just below the pelves was normal. The lower portions of the ureters were not visualized. The bladder was asymmetric, and there was a projection off the lateral superior portion that suggested a diverticulum. On July 17, a cystogram made with a 10 per cent solution of sodium iodide again demonstrated the deformity of the bladder (fig. 1).

Roentgen examination showed a deformity of the bladder most marked in the left upper portion, which suggested the possibility of a diverticulum in this region. This appearance may have been due to pressure on the right superior and posterior margins of the bladder. There was no evidence of a filling defect in the bladder itself. A roentgenogram of the chest made shortly after the patient's admission to the hospital showed increased pulmonary markings and no evidence of parenchymal disease; the appearance was that of any infection secondary to chronic disease of the upper respiratory tract.

A cystoscopic examination was made by Dr. Oscar Owre, on July 24. No obstruction was encountered when the cystoscope was inserted. The distending fluid contained clear epithelial tissue, sloughed from the ulcerating patches on the base of the bladder. At this stage, rectal examination was made, which revealed a markedly indurated growth lying external to the bladder, apparently growing between the rectum and involving the rectum and the bladder.

Urinalysis showed a persistent trace of albumin and normal specific gravity and concentration; the sediment contained from 5 to 10 red blood cells and from 30 to 40 white blood cells, per low power field.

Examination of the blood made on admission showed: hemoglobin, 88 per cent; red blood cells, 4,800,000; white blood cells, 6,500. The differential count revealed: polymorphonuclears, 58 per cent; lymphocytes, 39 per cent; eosinophils, 2 per cent and basophils, 1 per cent. On August 4, after the operation was performed, the hemoglobin was 90 per cent; red blood cells, 4,990,000 and white blood cells, 18,600; the differential count showed: polymorphonuclears, 91 per cent and lymphocytes, 9 per cent.

The Pirquet and Mantoux tests were negative. The Wassermann and Kahn tests were negative. Bleeding and clotting times were normal.

Postmortem Report.—The body was that of a well developed, and fairly well nourished white boy, 109 cm. in length, weighing about 23 Kg. Rigor and hypostasis were present. There was no edema of jaundice. Scattered over the chest and trunk were numerous light brown macules as described in the physical examination, and about fifteen subcutaneous nodules over the chest, trunk, neck and arms. These tumors ranged from the size of a pea to that of a bean; for the most part they were slightly raised above the surface, freely movable and firm in consistency. No tumors were found on the large peripheral nerves.

The peritoneal cavity contained about 75 cc. of thin, light brown fluid, and the peritoneal surfaces appeared normal. There was marked distention of the stomach and intestines. The appendix was retrocecal and normal. The tumor mass noted

Fig. 2.—Gross specimen cut, showing extensive neurofibromatosis with marked thickening of the wall of the bladder.

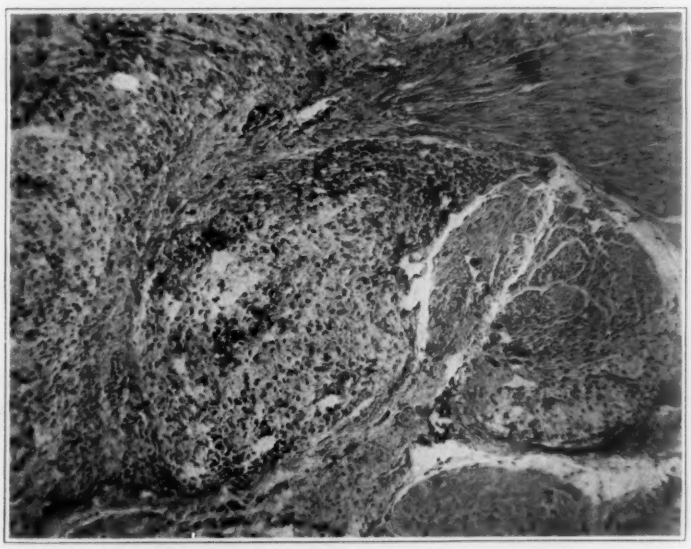

Fig. 3.—Photomicrograph of a section of the bladder showing neurofibroma between the muscle of the bladder. Hematoxylin-eosin stain; × 80.

clinically was found to be a large, thick-walled bladder. The maximum diameter of the bladder was 10 cm. and the maximum length 12 cm. The wall was markedly thickened in all parts, measuring from 2 cm. to 4 cm. Numerous tumors projected from the surfaces and extended somewhat into the adjacent perivesicular tissue; however, the bladder was easily dissected out. The greater growth of the tumors on the right caused the asymmetry noted in the roentgenogram. On section, it was found that the thick walls contained numerous firm grayish tumors, some of which were sharply circumscribed while others were rather diffuse. There was no obstruction of the urethral or ureteral openings. The rectum, when dissected away from the bladder, showed no involvement by the tumors. There was no other evidence of similar tumors within the abdominal or thoracic cavities.

The kidneys, ureters, bladder, prostate and rectum were removed together. The kidneys were of normal size and showed a moderate degree of cloudy swelling. The pelves and ureters of both kidneys showed no abnormalities. The bladder contained 100 cc. of urine clouded by postmortem desquamation of the epithelial cells. A trace of blood was present. There were several small superficial erosions at the base of the bladder. The prostate was normal.

Permission for examination of the head and spinal cord was refused.

Microscopic Examination.—Dr. E. T. Bell diagnosed sections of the tumor of the bladder and subcutaneous nodules as neurofibromas. Microscopic sections of the wall of the bladder under low magnification showed a tumor diffusely distributed throughout the musculature. The muscle was separated into large bundles by large cords of tumor tissue. The tumor tissue consisted chiefly of a rather loose areolar connective tissue in the form of fairly cylindric cords. In the central part of each tumor cord a bundle of nerve fibers could be seen. The distribution of the tumor was perineural throughout. In most places the structure of the tumor corresponded to that of a soft fibroma.

The following diagnosis was made: (1) scarlet fever, clinically; (2) bilateral bronchopneumonia; (3) pleurisy with effusion; (4) neurofibromatosis of the skin; (5) extensive neurofibromatosis of the bladder; (6) acute splenitis; (7) cloudy swelling of the liver and kidneys, and (8) multiple erosions of the bladder.

COMMENT

Despite the extensive neurofibromatosis of the bladder in the case reported, the kidneys, the ureters and the ureteral orifices were essentially normal, because there was no actual obstruction to the flow of urine. As a rule, hematuria, is not a prominent symptom in tumors of the bladder in children as it is in the adult. In the former, the tumors usually arise in the submucosa of the bladder and the mucosa remains intact.[14] In the case reported, bleeding was due to several small superficial erosions of the mucosa at the base of the bladder. Enuresis was probably a result of the involvement of the pelvic sympathetic innervation of the bladder and of the pressure exerted on the bladder by the invasion of the tumor.

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14. Helmholz, Henry F., and Amberg, Samuel: Diseases of the Genito-Urinary System in Infancy and Childhood, New York, D. Appleton and Company, 1930, vol. 19, p. 208.

A hereditary factor could not be demonstrated in our patient. He presented a typical picture of von Recklinghausen's disease with multiple nodules and pigmentary changes of the skin. The mental disturbances observed in cases of neurofibromatosis in children have been backwardness, changes in personality, defects of speech and apathy. Sensory changes, such as a feeling of numbness and dull pains in the extremities, may be present. Frequent headaches and aching pains in the extremities were symptoms in the case described.

Visceral neurofibromatosis, especially involvement of the bladder, is unusual in children.

SUMMARY

A rare case of neurofibromatosis, von Recklinghausen's disease, of the bladder with neurofibromatosis of the skin in a boy 7 years of age is reported. No previous report of the occurrence of a similar condition in children has been found in a search of the literature.

TRANSMISSION OF MALARIA BY TRANSFUSION

REPORT OF A CASE WITH TWO ACUTE DEVELOPMENTS OF THE DISEASE WHEN BLOOD FROM THE SAME DONOR WAS USED

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Transfusion of blood has become such a frequent therapeutic measure in the armamentarium of the pediatrician that it is now used almost as a routine measure by some clinicians. Transfusion is used in treating the moderately sick infant rather than as a final resort in an attempt to save one who is desperately ill.

Certain definite precautions are, or always should be, observed to protect the recipient against accident. These precautions especially include the grouping of the bloods, and, in some instances, direct typing to prove positive compatibility of the serums and cells. Another protective measure is the use of the Wassermann or a similar laboratory test to rule out syphilis.

There is never freedom from the possibility of the occurrence of an untoward accident in any technical procedure that deals with an organism as sensitive as the human being. It would be utterly impossible to rule out every known contingency.

The case that I shall report is one of malaria transmitted by the transfusion of blood from the father to his child on two different occasions, between which there was an interval of several months.

In a review of the literature, few cases of such accidental inoculation have been found; most of these reports have been published during the past three years.

In 1919, Grubb [1] reported the case of a British soldier who, as the recipient, transmitted malaria to a nursing sister who acted as donor. This type of accident is most unusual, and was due to faulty technic on the part of the surgeon. The following year (1920), Oehlecher [2] reported the occurrence of malaria in a father, aged 55, who had been the recipient of blood from his son who had never known of his malarial infection, but who had spent six years in West Africa, where he had taken 0.2 Gm. of quinine daily as a prophylactic measure.

From the Department of Pediatrics, University of Colorado School of Medicine.

1. Grubb, Alfred S.: Brit. M. J. **2**:74, 1919.
2. Oehlecher, F.: Deutsche med. Wchnschr. **46**:1025, 1920.

In 1920, van Dijk [3] also reported a case of malaria which developed in a patient suffering from influenza who had been given serum from a convalescent patient.

In 1927, Korabelnikoff [4] reported one case of his own, and mentioned another case reported by Sogua and Siebig and another by Hesse.

Flaum,[5] Schnitzler,[6] Chevallier and Schwob,[7] and Rosenthal,[8] all reported cases in 1929. Corvalho,[9] in 1930, reported a case of malaria transmitted from an infected donor. Decourt,[10] in 1931, related the occurrence of malaria in a patient given a transfusion from a person who had had a known infection nine years previously and who assumed himself to be free from the plasmodium, as he had had no symptoms in the interim. A few months prior to the writing of this paper, Jankelson [11] reported the case of a 6 weeks old infant in whom malaria developed after a transfusion of the blood from its Italian father. The latter had lived in Boston for twenty years, and had no clinical evidence of infection.

The case that motivates this report is of interest because malaria developed in a child on two different occasions following transfusion of blood from the same donor, her father.

REPORT OF CASE

History.—M. C., a girl, aged 2½ years, was admitted to the Denver General Hospital on July 23, 1929. The chief complaint was daily chills, followed by high fever and accompanied by profuse sweating.

The family history revealed that the father, aged 32, who was born in Greece, had come to this country when he was 16 years old. He could not recall having had malarial infection while in his native land. He had landed in New York, and had gone to Pittsburgh, where he had remained for three years. He emigrated to Dallas, Texas; as he had not been well, he consulted a physician, and a diagnosis of pulmonary tuberculosis was made. In 1921, while in San Antonio where he was confined to bed for treatment of the tuberculosis, severe chills and fever developed. The following year he came to Colorado in the hope that the climatic change would benefit him. He was in the tuberculosis pavilion of the Denver General Hospital for seven months, and was discharged as cured. He had never felt entirely well and normal, but managed to "drag along." He attended the

3. van Dijk, H.: Nederl. tijdschr. v. geneesk. **2**:1181, 1920.

4. Korabelnikoff, I.: Zentralbl. f. Chir. **54**:1218, 1927.

5. Flaum, E.: Wien. klin. Wchnschr. **42**:589, 1929.

6. Schnitzler, H.: Zentralbl. f. Chir. **56**:1438, 1929.

7. Chevallier, P., and Schwob, R.: Bull. et mém. Soc. méd. d. hôp. de Paris **53**:1189, 1929.

8. Rosenthal, G.: Bull. et mém. Soc. de méd. de Paris **16**:381 (Nov. 23) 1929.

9. Carvalho, C. R.: Bol. Soc. de med. et cir., São Paulo **13**:457, 1930.

10. Decourt, P.: Rev. de méd. et d'hyg. trop. **23**:32, 1931.

11. Jankelson, I. R.: Transmission of Malaria Through Injection of Whole Blood, J. A. M. A. **97**:177 (July 18) 1931.

outpatient department of the Municipal Clinic. Repeated examinations were made for the tubercle organism, and only once, in 1924, was the tubercle bacillus found. A Wassermann test of the blood made the same year was negative.

The mother, aged 31 years, who was born in Mexico of Spanish-American parentage, had had malaria six years prior to the child's admission to the hospital, when she was in Texas. Her first child died of malaria when 5 days old. Between her first and second child she had a miscarriage. She had been in good health since then, and later had been delivered of three normal children, including the patient.

There were two brothers, one older and one younger than the patient; both were apparently in good health.

The patient was born in a Denver hospital on Jan. 11, 1926, weighing 7 pounds (3,200 Gm.). At that time the Wassermann reaction of the blood was negative. Urinalysis showed the presence of albumin and many pus cells. When the patient was a little over a year old, she had measles, followed by bronchopneumonia.

On April 23, 1928, when she was 27 months old, she was brought to the dispensary because of high fever and diarrhea, which had been present for five days. She was slightly undernourished and pale, and appeared acutely ill. The rectal temperature was 103 F. There was a spontaneous cough and an occasional respiratory grunt. Examination of the chest showed decreased excursions, normal resonance, diminished breath sounds over both lungs and crepitant and subcrepitant râles, both anteriorly and posteriorly. Abdominal examination revealed no tenderness, mass or rigidity. The spleen was not palpable. The rest of the physical examination gave negative results.

First Admission.—The patient was admitted to the Colorado General Hospital with a diagnosis of bronchopneumonia, which was confirmed by roentgen examination. Improvement did not occur as rapidly as was expected. Two weeks after admittance, on May 8, another roentgenogram was made, and at that time the diagnosis was "probable pulmonary tuberculosis." No change was evident in roentgenograms taken on May 15, May 31 and June 14. Repeated examination of the sputum, and lavage of the stomach showed an absence of acid-fast organisms. On May 5, the Mantoux test was negative; on May 17, it was positive for bovine and human tuberculous infection. Another tuberculin test made on May 25 gave a questionable reaction, and on May 28 a Mantoux test was slightly positive to human tuberculin.

Slight improvement was noted in the general condition. On June 2, 160 cc. of citrated blood from the father were given intravenously. That evening the temperature rose to 103 F. Within three days the temperature was normal, and it remained so until the discharge of the child on June 14, fifty-four days after admission and twelve days after the transfusion.

On July 23, three months after the original admission and seven weeks after the transfusion, the mother brought the child to the outpatient department, because, except for the first week after leaving the hospital, about five weeks previously, she had not been well and had been having "chills and fever" with a temperature of 105 F. (axillary). At this time the spleen was greatly enlarged. The child was immediately admitted to the Denver General Hospital.

Examination.—Physical examination gave negative results except for a pale skin; hypertrophied tonsils; fine râles in the upper lobe of the left lung, anteriorly, and in the lower lobe, posteriorly, with diminished breath sounds throughout; a slight presystolic murmur which was heard best at the apex and transmitted toward the sternum; distention of the abdomen and enlargement of the spleen. A tentative diagnosis of pulmonary tuberculosis was made.

Course.—A roentgenogram showed bronchopneumonia and a moderately enlarged heart. The spleen was enlarged; the liver also showed some enlargement. The urine showed a few pus cells on several examinations. The hemoglobin was 70 per cent (Dare); the erythrocytes numbered 2,760,000; leukocytes, 8,100; polymorphonuclears, 59 per cent; large mononuclears, 1 per cent; small mononuclears, 38 per cent, and transitionals, 2 per cent. Malarial organisms of the quartan type were found in some of the erythrocytes. The temperature is demonstrated in chart 1. The day following admission, the child had a chill followed by high fever. On the two succeeding days, the temperature remained within normal limits. The following day, the child experienced another chill, followed by high fever. Malarial organisms were again demonstrated. There upon 2 grains (0.13 Gm.) of quinine was administered every eight hours. There were no more chills, and the child continued to improve. Several examinations of the blood revealed the absence of malarial organisms. By August 6, the spleen had decreased in size until it could be felt only on deep inspiration. The patient

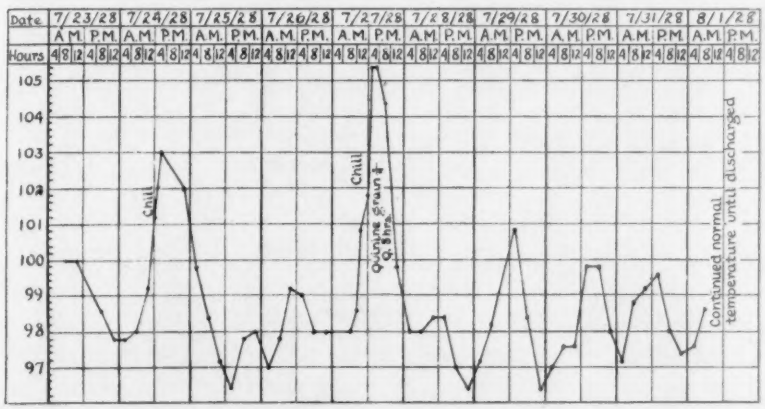

Chart 1.—Temperature curve typical of quartan malaria seven weeks after first transfusion.

was discharged on August 31, and told to take 2 grains of quinine daily for a month.

Second Admission.—On Feb. 19, 1929, the mother brought the child to the outpatient department with a temperature of 105 F. The patient was immediately admitted to the pediatric service of the Colorado General Hospital, with the chief complaints of high fever, discharge from the ears and malaria. The present illness had begun one week previously with fever, chills and sweating. This triad had been occurring daily. About the same time the ears had begun to discharge.

Examination.—The child was poorly nourished and pale. There was a profuse purulent discharge from the left ear; the right tympanum was injected and bulged slightly. The tonsils were enlarged and reddened. There was a slight mucopurulent discharge from the nasopharynx. There was considerable cervical lymphadenopathy. The lungs were resonant throughout; there were no râles, and no adventitious sounds were heard. The spleen was not palpable even under the most painstaking examination. Urinalysis showed albumin, + 1, and acetone, + 3. Examination of the blood showed: hemoglobin, 80 per cent (Dare);

erythrocytes, 4,260,000 and leukocytes, 25,600, with polymorphonuclears, 68 per cent; small lymphocytes, 31 per cent, and abnormal leukocytes, 1 per cent. No malarial organisms were found. In all other respects the physical examination gave negative results.

Course.—Chart 2 illustrates the curve for temperature during the stay in the hospital. Roentgenograms of the mastoids and the chest made on February 20 gave essentially negative results. The same day the urine showed: albumin, + 3; fine and coarse granular casts, + 3, and pus cells, + 1. The child did not improve as quickly as was expected, and with the change in the urinary observations, a transfusion of blood was done on February 25, the father again acting

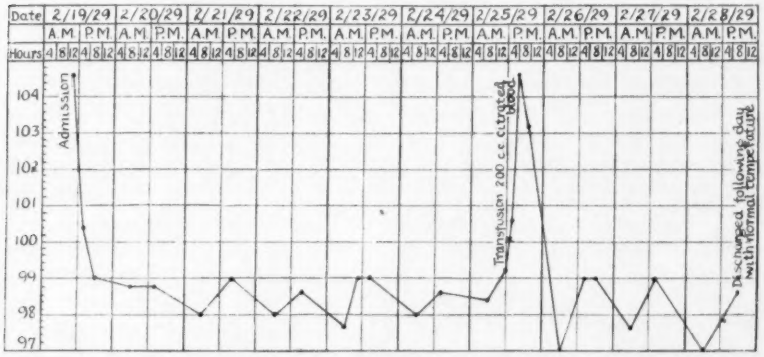

Chart 2.—Temperature curve, nonmalarial, at time of second transfusion.

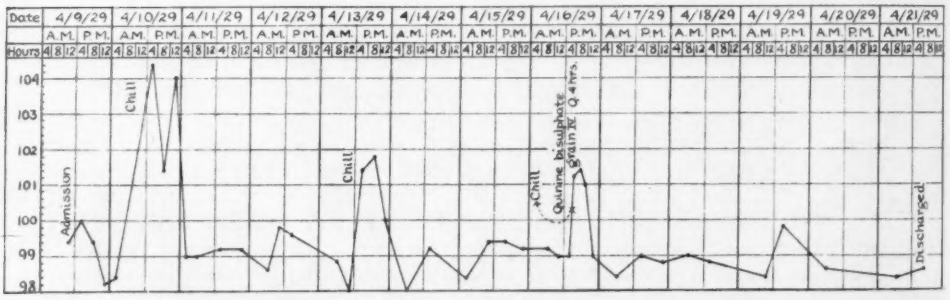

Chart 3.—Temperature curve again typical of quartan malaria five weeks after second tranfusion.

as donor. Two hundred cubic centimeters of citrated blood was given. This was followed by a chill lasting thirty minutes and a rise in the temperature to 104.4 F. The child's condition was improved on the next day. Urinalysis showed: albumin, + 2; casts, none; pus cells, + 1. Improvement continued, so that the patient was discharged after a stay in the hospital of eleven days.

The next appearance was five weeks after the transfusion, and the complaint was chills and fever in the evenings for the previous two weeks. According to the mother, these attacks occurred every evening. The spleen was definitely palpable. No malarial organisms were found on examination of the blood. On April 3, three days later, plasmodia again could not be demonstrated. On April 6, malarial

organisms of the quartan type were found. The child was admitted to the Colorado General Hospital, on April 9, with the diagnosis of malaria, quartan type.

Examination.—The physical examination gave normal results, except that the skin had a yellowish tinge throughout, and the spleen was palpated 3 cm. below the costal margin at the anterior axillary line. Urinalysis showed: albumin, + 1, acetone, + 1 and pus cells, + 1. Examination of the blood gave negative results, except for the presence of quartan malaria organisms.

Course.—Chart 3 shows the temperature. Plasmodia were found on the evening of April 9 and again on the following morning. The temperature rose to 104.4 F., on the afternoon of April 10. It was normal the next day, and remained so until April 13, when it rose to 101.8 F. After two days of freedom from fever, the temperature rose to 101.4 F. The clinical picture thus agreed with the laboratory diagnosis of malaria of the quartan type. The spleen was much larger than it was on April 10. Four grains (0.26 Gm.) of quinine bisulphate was given just preceding the expected chill on the afternoon of April 16 and every four hours thereafter. On April 19, there was no chill such as might have been expected if the medication had not been effective. On April 20, the spleen was definitely smaller. The patient was discharged the following day, as the temperature had been normal for five days. The medication was continued for several days following discharge.

On her return to the outpatient department seven weeks later, the spleen could not be palpated. There had been no further clinical evidence of malarial infection.

COMMENT

No case report could be found in the literature analogous to the one herein reported, in which malaria twice developed in a child after a transfusion of blood from her father. After the first development of the disease it was thought to be of congenital origin, as the mother gave a history of having had malaria six years before the first appearance of the disease in this patient, and the mother's first child was supposed to have died of the disease at the age of 5 days.

I feel safe in ruling out the congenital origin of the infection on the basis of the length of time elapsing between the birth of the patient and the appearance of the malaria, with nothing to suggest the possibility of the presence of the disease in the interim either in mother or child. Forbes [12] reported a case of congenital malaria which developed in an infant 7 weeks old born in Colorado of Greek parentage. The anopheles mosquito has never been found in eastern Colorado, according to Cockerell,[13] who made a thorough search for the insect.

When the disease occurred in the patient after the second transfusion from the same donor, it was felt that the source of the infection was fairly definitely proved. The mother's blood was examined for plasmodia, and no indication of infection was found. The father's

12. Forbes, R. P.: Congenital Malaria: Report of a Case in Colorado, Am. J. Dis. Child. **25**:130 (Feb.) 1923.

13. Cockerell, T. D. A.: J. Economic Entomol. **11**:195, 1918.

blood was also examined several times, even after he had been given strychnine, as advised by King,[14] Vecchia and Segre,[15] Silvestri [16] and di Pace.[17] On May 21, after suprarenal extract had been given as suggested by Dazzi,[18] one stippled red cell containing a body suggestive of malarial organisms was found. I was unable to obtain further cooperation from the father. The number of organisms present in the father's blood might be too few to be demonstrated easily by a smear, but the number of cells present in a transfusion of 200 cc. of blood would be sufficient to inoculate a recipient. When transplanted to a new soil with no natural immunity, organisms from a person in whom more or less tolerance for their presence had developed, thrived and produced the customary clinical evidence of the disease.

14. King, H. H.: Indian J. M. Research **6**:116, 1918.
15. Vecchia, E., and Segre, M.: Policlinico (sez. prat.) **25**:1081, 1918.
16. Silvestri, T.: Policlinico (sez. prat.) **26**:1418, 1919.
17. di Pace, I.: Policlinico (sez. prat.) **29**:1658, 1922.
18. Dazzi, A.: Policlinico (sez. prat.) **26**:1413, 1919.

Progress in Pediatrics

SICKLE CELL ANEMIA

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Since rational treatment may be developed only through a thorough knowledge of a disease, we are assembling and summarizing the information on the subject of sickle cell anemia, and including the reports of six cases that were studied at the Emory University Division of Grady (Municipal) Hospital in Atlanta.

HISTORICAL SURVEY

The disease was first described as a clinical entity by Herrick [1] in 1910. However, in 1904, Dresbach [2] reported a case of peculiar red cells occurring in a Negro medical student who turned in a sketch of his own blood as an assignment for laboratory work in histology. The instructor noted that the cells were drawn as elliptic rather than round shapes. This led to an investigation, and it was found that 90 per cent of the student's cells were elliptic, the length averaging two and a half times the width. At the time, the student had no symptoms, and his brother's blood was normal. Publication of this account caused considerable question and comment. Dresbach [3] showed the specimens to Ewing and Ehrlich, both of whom thought that the condition was of a congenital or developmental origin.

It is possible that the condition in Dresbach's case may have been an inactive type of sickle cell anemia. Ward,[4] however, classifies Herrick's anemia and Dresbach's syndrome as different types in the hemolytic jaundice group.

From the Emory University Division, Grady (Municipal) Hospital, Atlanta, Ga.

1. Herrick: Peculiar Elongated and Sickle Shaped Red Blood Corpuscles in a Case of Severe Anemia, Arch. Int. Med. **6**:517 (Nov.) 1910.

2. Dresbach: Elliptical Human Red Corpuscles, Science **19**:469 (March 18) 1904.

3. Dresbach: Elliptical Human Erythrocytes (A Supplementary Statement), Science **21**:473 (March 24) 1905.

4. Ward: Anemias of the Haemolytic Jaundice Group. Proc. Roy. Soc. Med. (Med. Sect.) **13**:1, 1919-1920.

Since the publication of Herrick's paper, more than forty cases of active sickle cell anemia have been reported, with mention of more than a hundred more. It is significant that only two cases have been reported outside of the United States. From Italy, Castana [5] reported an instance of a white child with semilunar gigantocytes, anemia and jaundice, which he uses as evidence that sickle cell anemia, a disease of Negroes, is not a clinical entity. Archibald's case [6] in an Arab has been accepted, but it must be remembered that Arabs are Caucasian and not negroid. In any event, in the light of our present knowledge, the disease is not limited to Negroes.

Abroad, some attempt has been made to familiarize the medical profession with the condition; in France this has been done by Comby [7] and Marie [8] by general discussion; in Germany, by Jaffe,[9] who reported two cases. However, sickle cell anemia remains primarily an American disease.

NOMENCLATURE

The disease was first known as Herrick's anemia, but this title was soon displaced by the more descriptive term of sickle cell anemia. When it was found that the blood of many apparently normal Negroes showed sickles, this condition was called latent sickle cell anemia. Objection was raised to that term on the grounds that the condition might never become active, and the word "sicklemia" was suggested. Because "sicklemia" is of mixed derivation, from Latin and Greek, Hahn and Gillespie [10] proposed the words, "drepanocyte," "drepanocytemia" and "drepanocytic anemia" for sickle cell, sicklemia and the active disease. Graham and McCarty suggested "meniscocytosis."

ETIOLOGY

Sickle cell anemia is primarily a familial disease, although sporadic cases occur. Huck [11] studied three generations in two families, forty-three persons in all, and concluded that the disease is transmitted by the mendelian law as a dominant factor. In sixteen of the reported

5. Castana, V.: Gigantocytes and Sickle Cells, Pediatria **33**:431 (April 15) 1925; abridged J. A. M. A. **84**:1966 (June 20) 1925.

6. Archibald: A Case of Sickle Cell Anemia in the Sudan, Tr. Roy. Soc. Trop. Med. & Hyg. **19**:389 (Jan.) 1926.

7. Comby: Anémie à cellules falciformes, Arch. de méd. d. enf. **31**:489 (Aug.) 1928.

8. Marie: L'anémie à hématies falciformes, Presse méd. **33**:678 (May 23) 1925.

9. Jaffe: Die Sichelzellenanämie, Virchows Arch. f. path. Anat. **265**:452, 1927.

10. Hahn, E. V., and Gillespie, E. B.: Sickle Cell Anemia, Arch. Int. Med. **39**:233 (Feb.) 1927.

11. Huck: Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **34**:335 (Oct.) 1923.

cases, one or more members of the patient's family were examined, and in these, sickle cells were found in nine instances.

Graham [12] noted a terminal streptococcus infection at several autopsies, and he is inclined to suspect this organism as an exciting cause of exacerbations of the disease. Hahn and Gillespie [10] obtained a pure culture of green-producing streptococcus from a spleen removed by operation. However, the importance of the streptococcus in the disease is yet to be determined.

The disease occurs more frequently in males than in females; 63 per cent of the reported cases occurred in males. It is also a disease of young people; only four cases have been reported in persons over

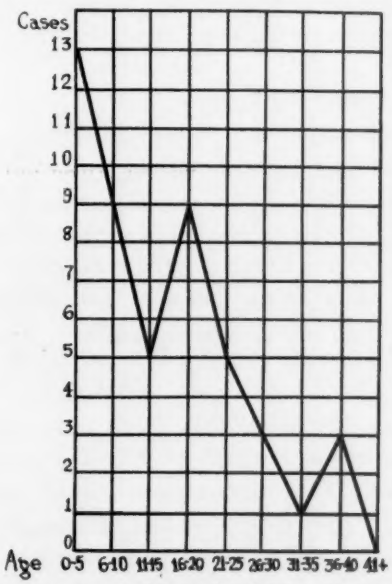

Chart 1.—Age incidence in sickle cell anemia.

30 and one in persons over 40. Sydenstricker [13] recognized sickle cells at birth in the blood of two babies born of mothers with sickle cells. The youngest patient with the active disease was an infant 7 months of age, whose case is reported in this paper. The low age incidence may be accounted for by the fact that the patients die early, generally of pulmonary infections or organic heart disease.

Until recently it was believed that only Negroes were susceptible to the disease, but in 1929, Cooley and Lee [14] reported an instance of

12. Graham, G. S.: A Case of Sickle Cell Anemia with Necropsy, Arch. Int. Med. **34**:778 (Dec.) 1924.

13. Sydenstricker, V. P.: Further Observation on Sickle Cell Anemia, J. A. M. A. **83**:12 (July 5) 1924.

14. Cooley, T. B., and Lee, P.: Sickle Cell Anemia in a Greek Family, Am. J. Dis. Child. **38**:103 (July) 1929.

the condition in a Greek boy who had no taint of Negro blood. His mother showed some sickling and a brother had cells resembling, but not typical of, sickle cells. However, in view of this case and the cases of Castana [5] and Archibald [6] previously mentioned, it must be granted that the disease may occur, if rarely, outside the Negro race.

Elliptic red cells are found in rare instances in the blood of normal white people, and this condition must not be confused with sickle cell anemia. Bishop [15] reported a case in a white woman whose blood showed from 70 to 80 per cent elliptic cells, but who did not have anemia. A sister's blood showed the same characteristics. The photographs suggest sickle cell anemia but do not present the typical picture. Huck and Bigalow [16] reported a similar case in a white medical student whose mother was found to have the same type of cells.

PATHOGENESIS

The change from round to sickle cells has been shown by Jaffe [9] to occur in the reticulo-endothelial system, especially in the spleen and, to a marked extent, in the bone marrow and the liver. He found 90 per cent of sickle cells in these organs and only 60 per cent in the other organs. Rice [17] stated that there is a congenital malformation of the splenic sinuses, allowing the free escape of the blood into the pulp. This is especially true around the malpighian bodies, which become almost surrounded by pools of blood.

The stage in the life of the erythrocytes at which sickling may take place in vivo is evidently early. Nucleated sickle cells have been seen by Cooley and Lee [18] and by Jaffe,[9] who have also noted sickle cells that were reticulated. This indicates a very early transformation.

The sickle cells appear to act as foreign bodies in the blood stream and are phagocytosed. Quantities of phagocytosed sickle cells are seen in the Kupffer cells of the liver,[19] and occasional ones are seen in monocytes.[20]

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15. Bishop, F. W.: Elliptical Human Erythrocytes, Arch. Int. Med. **14**:388 (Sept.) 1914.

16. Huck and Bigalow: Poikilocytes in Otherwise Normal Blood (Elliptical Human Erythrocytes), Bull. Johns Hopkins Hosp. **34**:390 (Nov.) 1923.

17. Rice: The Splenic Lesion in Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **43**:398 (Dec.) 1928.

18. Cooley, T. B., and Lee, P.: The Sickle Phenomenon, Am. J. Dis. Child. **32**:334 (Sept.) 1926.

19. Jaffe (footnote 9). Wollstein, M., and Kreidel, K. V.: Sickle Cell Anemia, Am. J. Dis. Child. **36**:998 (Nov.) 1928.

20. Archibald (footnote 6). Fradkin and Schwartz: Sickle Cell Anemia, J. Lab. & Clin. Med. **15**:519 (March) 1930. Huck (footnote 11). Jaffe (footnote 9).

A logical sequence of events is thus suggested: young erythrocytes are transformed into sickle cells in the spleen, liver and bone marrow, and as fast as they are released into the blood stream they are phagocytosed as foreign bodies. Ninety per cent of the supply of new red

TABLE 1.—*Observations on the Blood of Patients with Sickle Cell Anemia*

Case Number	Reference Number	Age	Sex	Red Cells, Millions	White Cells, Thousands	Hemoglobin, per Cent	Sickle Cells, per Cent	Nucleated Red Cells	Reticulocytes, per Cent	Platelets, Thousands	Van den Bergh Direct	Van den Bergh Indirect	Fragility	Urobilin	Family Affected
1.....	1	18	M	1.9	9	45	10	..	..	..	p	p	n	p	p
2.....	1	4	M	3.2	14	60	3	..	..	..	p	p	n	..	p
3.....	2	13	M	1.7	9	25	95	..	6	..	sp	p	d	..	p
4.....	3	10	M	2.5	25	45	75	p	..	..	..	..	n	p	n
5.....	4	1½	M	...	..	..	100	p	1.4	..	n	p	d	p	n
6.....	4	2½	F	0.9	44	20	90	p	40	130	n	p	d	p	p
7.....	8	24	M	2.2	24	40	100	p	..	..	n	p	d	..	..
8.....	11	21	F	2.4	12	48	33	p	..	..	..	..	..	..	p
9.....	12	3	F	2.7	..	55	p	..	p	..	n	p	d	p	..
10.....	12	5	F	2.7	..	55	p	p	p	..	n	p	d	p	p
11.....	14	13	M	2.4	12	40	80	p	3	..	sp	p	d	p	p
12.....	17	3½	M	3.7	14	62	p	p	p	..	n	p	n	p	..
13.....	19	26	F	2.3	12	36	98	p	14	120	n	p	d	p	n
14.....	20	30	M	2.8	45	48	98	p	18	400	n	p	d	p	..
15.....	23	1½	M	1.8	40	40	100	..	6	..	..	p	d	..	..
16.....	24	4	M	2.1	13	30	p	..	19	..	p	p	d	..	p
17.....	25	33	M	3.5	12	50	50	..	7	..	n	p	n	p	n
18.....	26	20	M	2.5	12	50	90	p	9	..	n	p	d	p	p
19.....	27	20	M	2.8	15	50	p	p	..	..	..	..	..	p	..
20.....	28	17	F	3.3	13	50	p	p	15	490	..	..	i	p	..
21.....	28	17	M	2.1	19	40	99	p	20	i	..	..	i	p	..
41.....	28	20	M	2.7	..	40	99	p	..	400	..	..	..	..	..
22.....	30	8	M	1.2	6	22	40	p	..	..	..	..	..	..	..
23.....	30	6	F	1.6	42	..	17	p	..	..	..	..	..	..	..
25.....	32	19	M	2.5	5	50	20	p	26	d	..	p	d	n	..
26.....	35	4	M	2.2	12	12	p	..	..	..	..	p	d	..	n
27.....	37	37	M	3.5	..	70	100	..	..	..	..	..	..	..	..
28.....	37	18	F	3.4	..	60	100	..	..	..	..	..	..	..	..
29.....	37	8	M	4	..	87	100	..	..	..	..	p	n	..	..
30.....	39	21	M	2.3	16	43	4	p	25	..	..	..	d	p	..
31.....	40	..	..	1.7	28	42	p	p	..	..	..	..	d	..	..
32.....	42	24	M	3.5	..	70	p	..	2.3	..	..	..	..	n	..
48.....	43	38	M	1.8	8	46	p	p	..	..	..	..	d	..	n
24.....	47	13	F	2.4	11	44	100	..	18	..	..	p	..	p	p
33.....	48	5½	M	1.3	64	25	20	..	19	..	..	..	d	p	p
34.....	48	6	M	1.5	20	38	27	p	34	..	..	..	d	p	p
35.....	49	15	F	2.7	12	60	75	..	..	..	p	p	i	p	n
36.....	51	38	F	2.3	..	43	p	p	10	..	n	p	..	..	..
37.....	52	6	M	...	..	..	100	..	15	244	n	p	d	..	p
38.....	54	25	F	2	11	50	p	p	..	..	..	..	..	..	..
39.....	55	4	F	2.5	..	40	100	..	..	..	..	..	n	..	..
40.....	55	3	M	...	..	..	100	..	..	..	..	..	..	..	..
49.....	55	4	F	...	..	..	..	..	..	..	..	..	..	..	..
42*.....	..	15	M	2	13	60	2	p	..	..	p	p	..	..	..
43*.....	..	16	M	2.3	11	50	48	p	..	..	n	p	..	..	..
44*.....	..	9	F	2.2	16	60	p	p	..	..	..	..	..	..	..
45*.....	..	28	M	3.1	45	65	23	p	..	..	n	p	d	..	..
46*.....	..	9	F	1.7	28	35	15	p	12	..	n	p	..	p	..
47*.....	..	½	F	1.5	9	40	95	p	24	..	n	p	d	..	..

* Cases reported in this paper.

† In the tables here presented, *p* means positive; *n*, negative; *sp*, slightly positive; *d*, direct, and *i*, indirect.

cells are sickle cells. When they are put into circulation, all except about 2 per cent of the sickle cells are destroyed by phagocytosis. This brings about a greater activity of the bone marrow in the production of new cells, as is indicated by the increase in reticulocytes. The spleen and liver enlarge to take care of the influx of young cells, and a vicious

cycle is established. As fast as the red cells form, they become sickle cells and are phagocytosed. The bone marrow cannot continue its hyperactivity indefinitely, and as the disease progresses, fewer new cells are put into circulation. The stimulus that caused the spleen to enlarge is thus removed, and it decreases in size. The liver, however, remains enlarged, possibly because its various other functions make it less responsive to the failure of the hematopoietic system. All of the common symptoms of the disease may be explained on the basis of the aforementioned theory.

The mechanism of the formation of the sickle cells has been the subject of considerable investigation. In 1917, Emmel [21] suggested that the formation of sickle cells might be due to an accentuation of the normal process that changes the original spherical cell into a biconcave disk.

Josephs [22] found that if the cells from patients with sickle cell anemia were washed six times through physiologic solution of sodium chloride they would not sickle. If, however, the cells were suspended in the previous washings or in normal serum, sickling occurred. From this observation, he concluded that an unknown substance common to all plasma is absorbed by the red cells and will cause some of the cells to sickle in sickle cell anemia; that the substance may be removed from the cells by repeated washings with saline, and that it is then present in the washings.

Hahn and Gillespie [10] devised a closed chamber in which cells could be saturated with various gases. They found that blood from patients with sickle cell anemia could be made to sickle immediately by saturation with carbon dioxide, and that the cells would revert to a normal shape when saturated with oxygen. Blood from patients with other types of disease or from normal persons did not behave in this manner. This work, which has been confirmed by other investigators, points to anoxemia as the precipitating cause of sickling. The fact that a pathologic condition of the lungs rather frequently accompanies the disease appears to lend additional weight to this theory.

Seeking further light on the theory, Dalgopal and Stitt [23] examined seventy-seven tuberculous patients; one had an active case of sickle cell anemia and in three the sickle cell trait was found. This incidence is 5.2 per cent, or slightly below the average incidence as determined

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21. Emmel, V. E.: A Study of the Erythrocytes in a Case of Severe Anemia with Elongated and Sickle Shaped Red Blood Corpuscles, Arch. Int. Med. **20**:586 (Oct.) 1917.

22. Josephs: Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **40**:77 (Feb.) 1927.

23. Dalgopal and Stitt: The Sickle Cell Phenomenon in Tuberculous Patients, Am. Rev. Tuberc. **19**:454 (April) 1929.

from the large series hereafter mentioned. Moreover, the patient with the active condition suffered no dyspnea and was not anoxemic, while one of the patients with an "inactive" case had severe tuberculosis without the development of active sickle cell anemia. It is thus evident that "chronic anoxemia caused by disease or compression of lungs is not a factor in development of active sickle cell anemia from sicklemia"; and the incidence of the disease is not greater in tuberculous patients than in the general population. This is another evidence of the variance between conditions *in vitro* and *in vivo*.

Opposed to the theory of anoxemia is the work of Hein, McCalla and Thorne,[24] who found that "blood taken under paraffin oil and kept under oil without exposure to air shows practically no sickling whatever." The experiments of Graham and McCarty[25] cast still further doubt on the theory of anoxemia. They took blood from patients with sickle cell anemia after death and sealed it in capillary tubes. No more sickling occurred than had been previously noted in the circulating blood. However, cover slip preparations of the same blood showed almost complete sickling in one hour. They also show that sickling occurs more readily when the blood is compressed between cover slips than when it is in a central well in which the pressure is not so great. From this they concluded that the sickle cell phenomenon is largely mechanical in origin rather than due to a relative deficiency of oxygen.

PATHOLOGY

The observations at autopsy of significance are limited to the spleen, the bone marrow and the liver.

Rice[17] believes that a congenital malformation of the splenic sinuses, with extravasation of blood into the pulp, is characteristic of the disease. He also noted an abnormal development of the capillaries in the malpighian bodies. In practically all of the reported autopsies there was distention of the splenic sinuses with red cells and atrophy of the pulp. The malpighian bodies are small,[26] and small hemorrhagic areas may be seen.[27] Graham[10] noted many sharply defined round areas of

24. Hein, McCalla and Thorne: Sickle Cell Anemia, with Report of a Case with Autopsy, Am. J. M. Sc. **173**:763 (June) 1927.

25. Graham and McCarty: Sickle Cell (Meniscocytic) Anemia, South. M. J. **23**:598 (July) 1930.

26. Jaffe (footnote 9). Sydenstricker: Sickle Cell Anemia, South. M. J. **17**: 177 (March) 1924. Sydenstricker, V. P.; Mulherin, W. A., and Houseal, R. W.: Sickle Cell Anemia: Report of Two Cases in Children, with Necropsy in One Case, Am. J. Dis. Child. **26**:132 (Aug.) 1923.

27. Hein, McCalla and Thorne (footnote 24). Sydenstricker: Sickle Cell Anemia, M. Clin. North America **12**:1451 (March) 1929. Sydenstricker, Mulherin and Houseal (footnote 26, last reference).

bright red, which he believed to be regenerative foci of hyperplastic splenic tissue. The spleen is dark red and firm; the capsule is rough and thickened. The size of the spleen varies widely. Steinberg [28] mentioned a spleen weighing only 2.4 Gm., whereas Landon and Lyman [29] reported the removal of one weighing 621 Gm.

The liver is nearly always enlarged; the sinusoids are somewhat dilated and contain many blood cells, both normal and sickle cells. Phagocytosis of the latter by Kupffer cells may be noted.

The bone marrow is hyperplastic, with a great number of sickle cells and nucleated red cells. Sydenstricker [30] also noted some elongated filiform cells, from six to twenty times as long as they were broad.

Huck [11] obtained a culture of hemolytic streptococci from an ulcer of the leg. The ulcers show no characteristic pathologic process.

Some question has been raised as to whether the sickle cells seen in fixed tissues might not be due to the reagents used. Graham [12] found whorls of sickle cells in bone fixed in Kaiserling's fluid unlike those fixed in Zenker's solution, and concluded that the deformity of the cells was due to the fixing agent. Hahn [31] found that formaldehyde gas fixed the sickle cells in their characteristic form, while Zenker's solution fixed cells in the round form. Jaffe [9] however, found sickle cells in tissues fixed by both methods. Graham and McCarty [25] recently suggested that the shape of the cells is due to the degree of tissue shrinkage rather than to the chemical nature of the fixing reagent. Nevertheless, the fact remains that sickle cells are found in the tissues of patients with proved sickle cell anemia, and that they are not found in every patient who comes to autopsy.

SYMPTOMATOLOGY

The signs and symptoms will be presented as summarized from the forty-nine reported cases. The patient usually gives a history of having been weak and sickly for a number of years and of having had previous attacks of weakness, jaundice, fever and abdominal or articular pain. There is usually a history of repeated acute infections of the respiratory tract. The course of such infections is generally longer than that in normal persons.

The most common physical findings, in order of frequency, are: greenish-yellow sclera, heart murmur, enlargement of the liver, adenopathy, enlarged heart, ulcer of the leg, pulmonary disease, enlarged

28. Steinberg, B.: Sickle Cell Anemia, Arch. Path. **9**:876 (April) 1930.

29. Landon and Lyman: Sickle Cell Anemia with Case Report of Splenectomy, Am. J. M. Sc. **178**:223 (Aug.) 1929.

30. Sydenstricker, Mulherin and Houseal (footnote 26, last reference).

31. Hahn: Sickle Cell (Drepanocytic) Anemia, Am. J. M. Sc. **175**:206 (Feb.) 1928.

spleen and infantile genitalia. The greenish-yellow tinge to the sclera is usually the only evidence of jaundice that can be noted in the Negro; in this disease it is indicative, of course, of an excessive destruction of red cells. The heart murmur may be merely functional from the anemia, but in many cases there is organic heart disease as well as sickle cell anemia. The liver is enlarged in 59 per cent of cases; an explanation for its enlargement was attempted in the discussion of pathogenesis. Adenopathy occurs chiefly in the cervical and axillary lymph nodes. When it is remembered that these nodes drain the respiratory tract, which is so frequently infected in these patients, the glandular

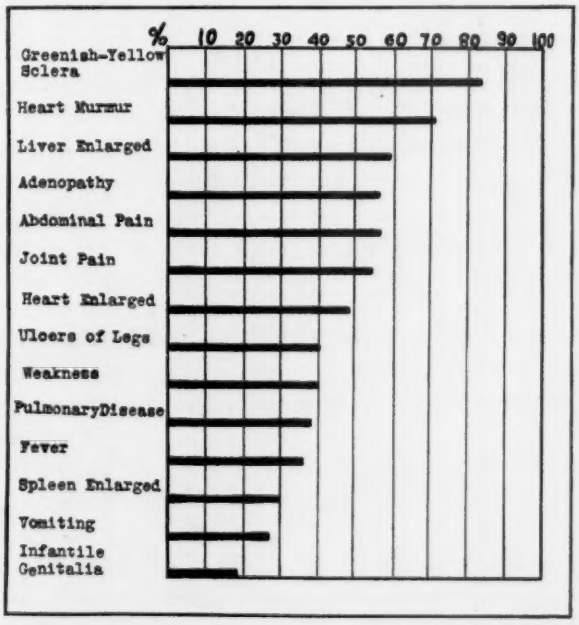

Chart 2.—Signs and symptoms of sickle cell anemia.

enlargement is explained. The heart is enlarged in 49 per cent of the cases. Ulcers of the legs have been regarded by some as an important factor in diagnosis, but they have occurred in only 40 per cent of the reported cases. Their occurrence may be due to the lowered resistance of the anemic patient, so that minor bruises and scratches refuse to heal properly. Pulmonary disease was found in 38 per cent of the cases; some of the patients had tuberculosis and some, heart failure, while others were admitted for pneumonia or bronchitis. A rather low percentage (only 30 per cent) showed enlargement of the spleen. It is significant that the average age of patients with enlargement of the spleen is 5 years, while the general average for all patients is 16

years. This gives a basis for the theory that the spleen becomes enlarged in the beginning of the disease and later atrophies. Infantile genitalia were noted in 18 per cent of the cases. It must be considered, though,

TABLE 2.—*Signs and Symptoms in Patients with Sickle Cell Anemia*

Case Number	Reference Number	Age	Sex	Abdominal Pain	Vomiting	Weakness	Fever	Joint Pain	Ulcers or Scars on Legs	Greenish Sclera	Pathologic Condition of Lungs	Heart Enlarged	Heart Murmur	Liver Enlarged	Spleen Enlarged	Adenopathy	Infantile Genitalia
1.....	1	18	M	p	..	..	..	..	p	p	n	p	p	p	n	p	p
2.....	1	4	M	p	..	p	..	..	..	p	p	p	p	p	p	..	..
3.....	2	13	M	n	..	p	..	..	..	p	n	p	p	n	n	p	..
4.....	3	10	M	..	..	..	p	..	n	p	n	..	p	p	p	p	p
5.....	4	1½	M	..	..	..	..	p	..	p	..	..	p	p	p	p	..
6.....	4	2½	F	p	..	..	..	..	n	p	p	p	p	p	p	p	..
7.....	8	24	M	..	..	p	..	p	p	p	p	n	p	p	n	p	p
8.....	11	21	F	..	..	..	..	p	p	p	n	..	p	..	n	..	..
9.....	12	3	F	..	..	..	..	..	n	p	..	..	..	..	n	n	..
10.....	12	5	F	..	..	..	..	..	..	p	..	..	..	..	n	n	..
11.....	14	13	M	..	..	..	..	..	n	p	..	p	p	p	n	..	..
12.....	17	3½	M	p	..	..	..	p	..	p	p	p	p	p	p	p	..
13.....	19	26	F	p	..	..	p	p	..	p	p	..	p	p	n	sp	..
14.....	20	30	M	p	..	..	p	p	p	p	p	p	n	n	n	..	..
15.....	23	1½	M	..	p	..	..	..	..	p	..	..	n	p	p	p	..
16.....	24	4	M	p	p	p	..	..	n	p	p	..	p	p	p	..	..
17.....	25	33	M	p	p	..	..	p	p	p	..	p	..	p	..	p	..
18.....	26	20	M	p	p	..	..	p	p	p	n	p	p	p	n	p	..
19.....	27	20	M	p	p	..	p	p	p	p	p	p	p	n	n	p	..
20.....	28	17	F	p	p	p	..	p	p	p	n	p	p	..	..	..	p
21.....	28	17	M	..	..	p	..	p	p	..	..	p	p	p	n	..	p
41.....	28	20	M	..	..	..	..	..	p	..	..	..	..	..	..	..	..
22.....	30	8	M	..	..	..	..	..	..	p	p	..	..	..	..	..	..
23.....	30	6	F	..	..	..	..	..	..	p	p	..	..	..	..	..	..
25.....	32	19	M	..	..	p	p	p	..	p	n	n	p	n	n	p	..
26.....	35	4	M	p	p	..	p	p	..	n	..	..	p	p	p	p	..
27.....	37	37	M	..	..	p	..	p	..	p	..	..	..	..	..	p	..
28.....	37	18	F	p	p	p	..	p	p	p	..	p	..	..	..	p	..
29.....	37	8	M	..	..	p	p	p	p	p	..	n	p	p	p	p	..
30.....	39	21	M	p	..	p	p	..	p	p	p	p	p	p	n	p	p
31.....	40	..	..	..	..	..	p	..	..	..	p	..	p	n	n	..	..
32.....	42	24	M	p	..	..	..	p	p	p	..	p	p	p	..	..	..
48.....	43	38	M	p	..	..	p	..	..	p	n	n	p	n	..	..	..
24.....	47	13	F	p	p	p	..	p	p	p	..	..	p	p	n	p	..
33.....	48	5½	M	p	p	..	p	p	..	p	n	p	p	p	n	p	..
34.....	48	6	M	p	..	p	p	..	..	p	p	p	p	p	p	p	..
35.....	49	15	F	p	..	p	..	p	..	p	..	..	p	p	n	..	..
36.....	51	38	F	..	..	..	..	..	p	p	..	n	n	n	n	p	..
37.....	52	6	M	p	..	..	p	p	..	p	..	p	p	p	p	..	..
38.....	54	25	F	p	..	p	p	..	p	p	..	p	p	n	p	p	p
39.....	55	4	F	p	p	..	..	p	..	p	..	..	..	n	p	..	..
40.....	55	3	M	p	p	..	p	..	..	p	p	n	p	p	p	..	..
49.....	55	4	F	p	p	..	..	..	..	..	..	..	..	p	n	..	..
42*.....	..	15	M	p	..	p	..	p	p	p	p	p	p	p	n	n	p
43*.....	..	16	M	..	p	p	..	p	p	p	p	p	p	p	n	p	p
44*.....	..	9	F	p	..	p	p	p	n	..	p	p	n	n	n	p	..
45*.....	..	28	M	n	n	p	..	p	p	..	p	p	p	p	n	p	..
46*.....	..	9	F	p	..	p	p	p	n	p	p	p	p	n	n	p	..
47*.....	..	½	F	..	..	p	p	..	n	..	p	n	n	n	p	p	..

* Cases reported in this paper.

that the infantile character of the genitalia will hardly be noticed until the child reaches puberty. If patients under 10 years of age are not considered, it may be said that 26 per cent show infantile genitalia. This condition could easily result, however, from the anemia and general underdevelopment.

The blood picture is the most characteristic and diagnostic feature of the disease. The anemia tends to be progressive, and in the late stages the red cell count may be less than 1,000,000. The average count in this disease is from 2,000,000 to 2,500,000, though occasionally it is as high as 3,500,000. The hemoglobin varies in proportion to the red cells, averaging around 40 to 50 per cent. Nucleated red cells are generally seen, and the percentage of reticulated red cells is increased to from 10 to 15 per cent or more in most cases. Sickle cells are present, of course, and constitute the basis for diagnosis. The number of sickle cells seen in stained smears, representing the number of these cells actually present in the blood stream, varies from 0.5 to 4 per cent in the average case. Moist preparations of fresh blood, incubated for from six to twenty-four hours, show from 50 to 100 per cent sickle cells. Hahn [31] pointed out that the severity of the disease is proportionate to the number of sickle cells in the circulating blood rather than to the number formed in vitro. There is a moderate leukocytosis, polymorphonuclears predominating, arising from the general hyperactivity of the blood-forming organs.

The van den Bergh test shows a positive reaction in the indirect phase, varying from a trace to 10 units. The direct van den Bergh test is only occasionally positive.

The resistance of the red cells to hemolysis by hypotonic salt solution is either normal or increased. In three cases a slight increase in fragility was noted, but in the majority of cases the range of resistance was increased.

Platelet counts were made in a few instances, but they are not informative, as some show an increased, some a decreased, and others a normal, count.

Urobilin is often to be found in the urine. This is the expected consequence of the hyperbilirubinemia indicated by the van den Bergh test.

Moore [32] described roentgenologic findings in the bones of a patient with sickle cell anemia, which he believes to be typical of the disease. The parietal bones were 100 per cent thicker than the other bones of the skull, the increase of thickness being chiefly confined to the diploe and being marked with radial striations. The radii and long bones of the hands and feet showed a marked decrease in the marrow cavity. Moore stated that the observations on the skull appear to be the same as those found in von Jaksch's anemia, but that the changes in the bones of the appendicular skeleton "constitute an additional point of destruction."

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32. Moore: The Bone Changes in Sickle Cell Anemia with Note on Similar Changes Observed in Skulls of Ancient Mayan Indians, J. Missouri M. A. **26**: 561 (Nov.) 1929.

DIAGNOSIS

The diagnosis rests on finding the characteristic sickle cells and the presence of chronic anemia. Since relatively few sickle cells are seen in the stained smear, even in severe cases, the abnormality may be overlooked unless a fresh preparation is examined. Emmel [21] discovered that blood which showed no sickle cells in the stained smear might show such forms if sealed under a cover slip with petrolatum and incubated at room temperature for twenty-four hours. This method, with slight modifications, has been in use since then. Graham and McCarty [25] suggested the use of a number 0 cover slip instead of the customary number 2. The authors have found immersion oil more convenient than petrolatum for sealing the cover slip to the slide.

A fresh preparation made by Emmel's method will show from 40 to 100 per cent sickle cells after from four to twenty-four hours, and the diagnosis is easily established.

The characteristic and unmistakable sickling readily eliminates anemia of any other type from the differential diagnosis.

TREATMENT

The treatment for sickle cell anemia is still in the experimental stage. The acute exacerbations appear to be benefited by rest in bed and supportive treatment. Transfusions cause only temporary improvement.

Splenectomy was advocated on the basis that the spleen destroyed the red cells, and in 1927 Hahn and Gillespie [10] made the first report on splenectomy. One month after operation the red count and fragility test gave normal results, and the van den Bergh reaction was negative. Since then six other splenectomies have been performed, and it has been found that while there is temporary improvement, the patient gradually sinks into his previous condition in from four to twelve months. Patients continue to show sickle cells after splenectomy.

Sydenstricker [33] did not obtain favorable results from treatment with liver, nor was that type of treatment successful in our experience. Levy,[34] however, obtained strikingly good results in three patients treated with the Minot-Murphy liver diet. His patients gained weight and strength, and the red cell count returned to normal. One patient stopped taking liver and the red cell count fell, but increased to normal again when the liver diet was resumed, although sickle cells persisted in diminished quantities.

The liver diet appears to offer more hope than any other treatment known at present, and deserves a thorough trial.

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33. Sydenstricker (footnote 27, second reference).
34. Levy: Sicklemia, Ann. Int. Med. **3**:47 (July) 1929.

PROGNOSIS

Because of their general weakness and lack of resistance, patients with this condition easily succumb to the various intercurrent illnesses to which they are subject. Few live beyond the age of 30 years.

THE SICKLE CELL TRAIT

Sickle cells are found in the blood of healthy Negroes. Graham and McCarty [25] examined the blood of 1,500 patients in routine hospital practice, and found that in 8.13 per cent the blood showed sickling in fresh preparations. Other observers [35] have reported smaller series. Of the grand total of 3,113 specimens of blood examined, 7 per cent showed sickle cells without any evidence of sickle cell anemia. The average red count of 61 of these patients [36] was over 4,000,000, with 70 per cent hemoglobin.

These reports were made from all parts of the country, so it appears that drepanocytemia is a racial characteristic affecting a proportion of all Negroes. This condition appears to have no bearing on the longevity or general health of the affected Negroes. There is no evidence that drepanocytemia ever becomes active drepanocytic anemia.

REPORT OF CASES

CASE 1.—*History.*—J. B., a colored boy, aged 15, was admitted to the hospital on Dec. 8, 1926, complaining of shortness of breath, weakness and abdominal pain. He gave a history of having had frequent attacks of migratory rheumatism followed by attacks of weakness and dyspnea since he was 3 years of age. He had also had irregular attacks of abdominal pain, apparently not related to the other conditions.

Physical Examination.—The patient was well developed, well nourished and moderately orthopneic, with a pulse rate of 100 and a temperature of 99.2 F. The conjunctivae were slightly jaundiced; the heart was greatly enlarged, with a rumbling systolic murmur at the apex; the lungs showed many moist râles at the bases; the spleen was palpable 2 cm. above the umbilicus; the liver was greatly enlarged; the penis was small, and no pubic hair was present; a number of scars from healed ulcers were seen on both legs, and moderate pitting edema of the feet and ankles was present.

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35. Cooley and Lee (footnote 18). Huck (footnote 11). Josephs: Clinical Aspects of Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **43**:397 (Dec.) 1928. Lawrence: Elliptical and Sickle Shaped Erythrocytes in the Circulating Blood of White Persons, J. Clin. Investigation **5**:31 (Dec.) 1927. Levy (footnote 34). Miyamata and Korb: Meniscocytosis (Latent Sickle Cell Anemia); Its Incidence in St. Louis, South. M. J. **20**:912 (Dec.) 1927. Smith: Sickle Cell Anemia, M. Clin. North America **11**:1171 (March) 1928. Wollstein and Kreidel (footnote 19, second reference).

36. Cooley and Lee (footnote 18). Levy (footnote 34). Miyamata and Korb (footnote 35, sixth reference).

Laboratory Data.—Laboratory tests showed: red cells, 2,070,000; hemoglobin, 60 per cent; white cells, 13,450. The differential count was normal. From 1 to 2 per cent of the red cells were sickle cells; 3 per cent were nucleated red cells; chemical examination of the blood gave normal results; the van den Bergh test was positive in the indirect phase; and a Wassermann test of the blood was negative. Urinalysis showed: specific gravity, 1.011, albumin, 4 plus, many granular casts, a few red blood cells and many pus cells. Phenolsulphonphthalein was 20 per cent the first hour and 10 per cent the second hour. A teleoroentgenogram of the heart showed mitral hypertrophy.

Course.—The temperature reached normal on the third day, and the patient left the hospital. On June 15, 1927, he was readmitted with the same complaint, but he left the hospital the next day without permission. On November 9, he was admitted with advanced heart failure, and died six hours later. Autopsy was not obtained.

A diagnosis of mitral heart disease with failure and sickle cell anemia was made.

CASE 2.—*History.*—E. L., a colored boy, aged 16, weighing 75 pounds (34 Kg.), was admitted to the hospital for study on May 16, 1927. He had always been undersized. He had had two severe cases of pneumonia with prolonged convalescence, influenza and frequent sore throat. For the past two years he had had recurrent attacks of pains in the joints. He became nauseated and vomited easily.

Physical Examination.—The patient was an underdeveloped Negro boy in no distress; the temperature and pulse rate were normal. The sclerae were greenish-yellow, the mucous membranes pale, the tonsils enlarged and inflamed and the cervical and axillary lymph nodes palpable. The heart was slightly enlarged; there was a systolic murmur at the apex, which was transmitted to the axilla; a few fine crackling râles were heard at the base of the left lung; the liver extended 3.5 cm. below the costal margin in the right mammary line; the spleen was not felt; the genitalia were infantile; pubic and axillary hair was absent. There were several scars and one healing ulcer over the anterior surfaces of the tibiae.

Laboratory Data.—Examination of the blood showed: red cells, 2,390,000; hemoglobin, 50 per cent; white cells, 11,700. The differential count showed 74 per cent polymorphonuclears; 48 per cent sickle cells (moist preparation), and 3 per cent nucleated red cells. An indirect van den Bergh test gave a delayed positive reaction; the Wassermann reaction of the blood was negative. The urine was positive for bile. The result of the test for albumin was 2 plus and there were a few hyaline casts.

Course and Diagnosis.—The patient was put on a general diet, being given 200 Gm. of liver daily. The temperature and the pulse rate remained normal. He left the hospital on May 23, one week after admission. No improvement was noted. A diagnosis of sickle cell anemia was made.

CASE 3.—*History.*—S. J. M., a colored girl, aged 9, was admitted to the hospital on July 20, 1927, with the complaint of drowsiness, convulsions and fever for the past two weeks. She had had periodic attacks of pains in the joints since she was 2 years of age.

Physical Examination.—The patient was a well developed and well nourished, rather unintelligent child with a temperature of 100 F. and a pulse rate of 98. The throat was slightly inflamed, and the cervical nodes were enlarged. Gonorrheal vaginitis was present.

Laboratory Data.—Examination of the blood showed: red cells, 2,250,000; hemoglobin, from 40 to 50 per cent; white cells, 16,800, with polymorphonuclears

predominating, and many sickle cells in stained smears. Urinalysis showed a few pus cells; a vaginal smear showed gonococci, and the Wassermann test of the blood was negative. The temperature became normal after three days, and the patient was dismissed because of gonorrhea. She had no convulsions while she was in the hospital.

Second Admission.—The patient was admitted for the second time on Aug. 15, 1928; she was unconscious, following a convulsion just before admission. For the past two days she had complained of pain in the stomach. Physical examination showed a temperature of 100 F. The eyes were normal; the lungs showed a few râles; the heart was slightly enlarged, with no murmurs; the liver and spleen were not felt; the genitalia were normal; the pathologic reflexes were absent, and there were no scars or ulcers on the extremities. Examination of the blood showed: red cells, 3,410,000; hemoglobin, 60 per cent; white cells, 23,150; a normal differential count, with 9 nucleated red cells to 100 white cells. Sickle cells were seen in a stained smear.

The temperature mounted rapidly to 104.6 F., and the patient died after two days.

Autopsy.—Autopsy performed by Dr. Norris showed bronchopneumonia and massive focal necrosis in the lungs. The liver was enlarged and showed considerable congestion and many sickle cells. The spleen was enlarged and fibrosed, weighing 400 Gm.; it showed considerable fibrosis of old calcified infarcts and numbers of sickle cells. The splenic capsule was considerably thickened. The bones showed large areas of necrosis. Some of the haversian canals were packed with sickle cells.

Diagnosis.—A diagnosis of sickle cell anemia, jacksonian epilepsy and bronchopneumonia was made.

CASE 4.—*History.*—O. D., a colored man, aged 28, was admitted to the hospital on Oct. 26, 1926, complaining of pain in the joints and weakness. At the ages of 10, 18, 24 and 27 he had had attacks similar to the present one. During two of these attacks he had "crops" of ulcers on the legs. For the past year he had not been able to work because of weakness. He had been subject to frequent colds and sore throat, and had had pneumonia and influenza. He had had three enlarged lymph glands of his neck removed. A brother had died of tuberculosis.

Physical Examination.—The patient was well developed and well nourished; the temperature and the pulse rate were normal. There was an icteroid tint to the sclera and roof of the mouth. Glands, varying in size from that of a pea to that of a walnut, were palpable along the cervical incisions. The lungs were normal on physical examination; the heart was slightly enlarged, and a short systolic pulmonic murmur was heard; the liver was greatly enlarged, and the spleen was not felt. There were numerous scars over both tibiae. External and internal hemorrhoids were present and bled slightly on manipulation.

Laboratory Data.—Examination of the blood showed: 3,100,00 red cells; 65 per cent hemoglobin, and 45,000 white cells. The differential count was normal, and 20 per cent of the cells were sickle cells. There were many nucleated erythrocytes. The van den Bergh test gave a delayed positive reaction in the indirect phase; the Wassermann reaction of the blood was negative. Hemolysis began at 0.33 and was not complete at 0.15. The urine was normal. A roentgenogram of the chest showed cardiac hypertrophy and pulmonary congestion suggestive of tuberculosis.

Course.—The patient had a slight fever (from 99 to 100 F.) for a week, and was afebrile for the remainder of his stay in the hospital. At the end of a month, the erythrocyte count was 2,600,000 and the white count, 7,500. Splenectomy was

performed by Dr. Boland on November 24. The spleen was very small and bound down by adhesions. The patient was in a fair condition after the operation but he died rather suddenly six hours later. A diagnosis of sickle cell anemia, with death from delayed shock was made.

CASE 5.—*History.*—I. J., a colored girl, aged 9, was admitted to the hospital on Oct. 29, 1926, complaining of weakness and pain in the hip. She had been admitted to the hospital three times in the past three years for bronchopneumonia, mitral heart disease with failure and hemiplegia of undetermined origin. Sickle cell anemia was not recorded on the previous admissions, but note was made of abnormally shaped erythrocytes, suggestive of those in pernicious anemia.

Physical Examination.—Examination showed: slight jaundice, an enlarged heart with a mitral systolic murmur and an enlarged tender liver. The spleen was not felt, and there were scars over both tibiae.

Laboratory Data.—Examination of the blood showed: red cells, 2,270,000; hemoglobin, 60 per cent; white cells, 20,000, with 80 per cent polymorphonuclears. Fifteen per cent of the cells showed sickling. The van den Bergh test was positive in the indirect phase. The urine was normal.

Course.—The patient had a remittent fever for three weeks and, becoming normal during the fourth week, was dismissed on November 30, improved. She was readmitted on June 16, 1927, for observation. At this time the picture was essentially the same, with the addition of enlarged cervical nodes. Blood counts showed, on the average, 3,500,000 red cells, 50 per cent hemoglobin, 13,000 white cells, from 2 to 4 nucleated red cells per 100 white cells and 12 per cent reticulocytes. Urinalysis showed an excess of urobilin. The patient was dismissed on July 9, improved. A diagnosis of mitral heart disease and sickle cell anemia was made.

CASE 6.—*History.*—M. D., a colored girl, aged 7 months, was admitted to the hospital on Feb. 27, 1931, with the complaint of continually shaking her head from side to side. She had been in good health until three weeks before admission, when a severe cold in the head developed. One week before admission she began to roll her head; she continued to take her food well.

Physical Examinataion.—Physical examination gave normal results, except for palpable epitrochlear and cervical nodes and a moderately enlarged spleen.

Laboratory Data.—Examination of the blood showed: red cells, 2,550,000; hemoglobin, 60 per cent; white cells, 9,500; polymorphonuclears, 44 per cent; large lymphocytes, 20 per cent, and small lymphocytes, 36 per cent. Moist preparation showed 60 per cent sickle cells in six hours and 95 per cent in twenty-four hours; there were 24 per cent reticulocytes; the indirect van den Bergh test was positive; a fragility test showed 0.34 to 0.26 (control blood hemolyzed at 0.42 to 0.32); the Wassermann test of the blood was negative; the calcium and phosphorus content of the blood was normal; the urine was normal, and roentgenograms of the long bones showed early rachitic changes.

Course.—The patient was given liver extract in milk. After a week the reticulocytes had risen to 64 per cent. A few nucleated erythrocytes were then seen. The erythrocyte count, however, gradually fell to 890,000 two days before death. The patient lost weight slowly but steadily. On April 2, bronchopneumonia developed, and she died the following day. Autopsy was not performed.

Progress in Pediatrics

CALCIUM AND TETANY IN FOLK MEDICINE

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The first "empiric" use of calcium for the alleviation of tetany is usually ascribed to Walter Harris. In 1689, in his treatise, "De Morbis Acutis Infantum," [1] he described a case of infantile convulsions and an "accomplished cure with no other medicines than a few ounces of crabs' eyes mixed with crystals of tartar." It is questionable, however, whether Harris deserves the credit for the use of testaceous or shell remedies *specifically* for tetany. According to Shipley,[2] "there was nothing new in the use of alkaline shells and stones in therapeutics. Harris merely increased the doses in which they were given and widened their field of use till it covered the whole field of pediatrics." It is more likely that Harris administered crabs' eyes (gastroliths of the common crayfish) to the little daughter of Goodman James Lowry as a purgative and as an antidote for "acidity of the Humours," rather than for the control of tetany, for he says: "The antecedent and the more distant Causes of the Diseases of Infants, however numerous they may be, all center, at least, in one immediate Cause, viz. in an acid prevailing through the whole Habit . . . In short, all the Complaints of Infants spring from an Acid as their common Source."

How and when calcium came into use as a *specific* remedy for tetany is not definitely known. Its rational use as an anticonvulsant probably originated with Sabbatini [3] as late as 1901, and calcium chloride was first used specifically for infantile tetany by Netter [4] in 1907. That the use of shells in the treatment of tetany among Negroes of the eastern shore of Maryland dates back many years is exemplified by the following anecdote:

In the course of obtaining the history of a Negro child brought to the Harriet Lane dispensary by its great grandmother, the information was obtained that

From the Harriet Lane Home of the Johns Hopkins Hospital and the Department of Pediatrics of Johns Hopkins University, Baltimore.

1. Harris, W.: De Morbis Acutis Infantum, London, S. Smith, 1689.
2. Shipley, P. G.: Ann. M. Hist. **4**:189, 1922.
3. Sabbatini, L.: Arch. ital. di biol. **34**:417, 1901; J. Physiol. internat. **30**:2, 1901.
4. Netter, A.: Compt rend. Soc. de biol. **62**:376, 1907.

the child had the "spasms" when about 1 year of age. When asked what had been done to alleviate the spasms, the old Negress refused to disclose the nature of the remedy, which she claimed to be a family secret, handed down from generation to generation. On her next visit to the dispensary, she was persuaded to divulge the secret on the condition that it would not be told to other Negroes. Her remedy was as follows: Two large oyster shells are cleaned and boiled until the organic matter has dissolved. The residue is dried, pulverized and dissolved in the patient's urine. This solution is administered in teaspoon doses, every hour, until the "spasms" disappear.

It is obvious that the remedy consisted of calcium carbonate dissolved in urine, and that it differed little from Harris' therapeutics, for he also preferred oyster shells to other lime-bearing substances. "If in such a variety of Testaceous Medicines almost of the same Nature any of them were to be preferr'd to others for their Virtues, I wou'd chiefly recommend common Oyster-shells, as they are found on the Sea Shoare after they have been long exposed to the Sun, and ripened, as it were, by his kindly Beams."

Folk medicine, of the practice of which this is an example, takes its origin from two sources. (1) The remedies may originally have been selected, after trial and error, by lay practitioners of medical magic from among the substances of vegetable, mineral and animal origin that came to their hands, or (2) they may have been adapted from recipes that were found to be efficacious in the hands of physicians. Apparently the laity remained faithful to these prescriptions long (often for centuries) after their use had been abandoned and forgotten by the profession that originated them. It is possible that the use of lime shells as an empiric remedy for convulsions was introduced into the eastern shore by English physicians who settled there in the seventeenth and eighteenth centuries. The influence of English medicine in that section of the eastern seaboard is also exemplified, according to Shipley,[5] in the use of such terms as "running ranges" or "runnin' reins," which has been distorted from the Elizabethan medical English, "running of the reins," to designate gonorrhea.

5. Shipley, P. G.: Personal communication.

News and Comment

GENERAL

Bequests and Donations.—The Shriners' Hospital for Crippled Children, Springfield, Mass., received $15,000 by the will of Mrs. Ella M. Johnson.

The James Whitcomb Riley Hospital for Children, Indianapolis, was bequeathed $5,000 by Mrs. Mary J. Procter.

The Children's Hospital, Detroit, received $10,000 by the will of Mrs. Adeline Livingstone, Detroit.

The Home for Destitute Crippled Children, Chicago, was given $10,000 by Mr. Martin A. Ryerson.

Fourth International Pediatric Congress.—Any American authors who would like to read papers at the meeting of the Fourth International Pediatric Congress in London, July 20 to 22, 1933, should submit abstracts of such papers to Dr. Henry Helmholz, Rochester, Minn., as soon as possible.

Staff Changes.—Dr. Louis C. Schroeder, director of the American Child Health Association, has been appointed director of the pediatric service at the New York City Nursery and Child's Hospital, to succeed Dr. Oscar M. Schloss. The pathologic laboratory at the hospital is now under the direction of Dr. Frederick A. Hemsath, formerly chief pathologist of the Lying-in Hospital.

La Rabida Jackson Park Sanatorium Dedicated.—The new La Rabida Jackson Park Sanatorium, Chicago, where free treatment is given children with heart disease, was dedicated on October 18. The medical director is Dr. Robert A. Black. The building cost about $300,000 and has accommodations for about 175 children.

SOCIETY NEWS

California White House Conference.—The California White House Conference on Child Health and Protection was held in San Francisco on November 11 and 12. Later meetings will be held at Los Angeles, Oakland, Fresno and Sacramento, Calif.

Illinois State Medical Society.—The Society is contemplating a definite program for the care of physically handicapped children in the state. This is to be carried on through its county societies.

UNIVERSITY NEWS

Dr. Jean Crump has been promoted to assistant professor of clinical pediatrics at the Woman's Medical College of Pennsylvania, Philadelphia.

DEATHS

Dr. Irving Snow, a well known pediatrician of Buffalo, died on Oct. 17, 1932.

Pediatric Biographies

JACOBIUS TRUNCONIUS

JOHN RUHRÄH, M.D.
BALTIMORE

The quest for pediatric poems leads one to Jacobius Trunconius, who, if he did not write a poem, served at least as an inspiration for one containing a clever list of the diseases of early life. This was written by some anonymous friend and appears in Trunconius' book on children which, together with a work on plague, is about all the record that Trunconius left, despite the assertion that glory shall shine on him forever and ever, unchecked by bounds of earth or sky or sea.

Trunconius lived in the latter half of the sixteenth century and practiced medicine in Florence. He is described on the title pages of his books as a philosopher and physician. That he was interested in pediatrics is evidenced by the fact that he wrote "de custodienda puerorum sanitate, ante partum, in partu et post partum." This was a collection of material which he admits having taking from the earlier writers. It included, as the title indicates, instructions on the care of the child before, during and after birth as well as accounts of measles, smallpox and other diseases. It contains nothing remarkable but the poem, which should be included in the list of those already considered in these articles.

The English rendering is by George Frederick Still, professor of diseases of children in King's College Hospital in London. He used it in his "History of Paediatrics" and has given permission for its use in the present instance. The original and the translation need no comment.

Excelsos tibi Lucinae Junonis honores
Mandanti nitidis, Trunconi docte, papyris
Assurgunt patres, queis dulcia pignora curae
Atque amor est charae sobolis studiumque nepotum;
Assurgunt itidem dulces expertae hymenaeos
Matronae foetum et partus quod ferre labores
Perdiscant, cuncti per quos discerpier artus
Dura et creduntur late ossa dehiscere hiatu;
Sed mage nascentum devincta est turba quod amplum
Pandis iter dias ipsis in luminis oras,
Irrumpant facile ut thalamos et vincula solvant,
Et nati vegetam attingant longamque senectam
Omnibus erepti qui membra tenella lacessunt
Atroces morbi, macies, seniumque Philippi
Atque *ὑδροκέφαλος* vastus capitis tumor, et qui
Per totum informes erumpunt corpus achores

IACOBI TRVNCONII PHILOSOPHI AC MEDICI

De cuſtodienda Puerorum Sanitate.

Ante Partum, in Partu, & poſt Partum

De curandis eorumdem morbis ex Hippocrate, quouſque Caninos Dentes emiſerint.

ACCESSIT

Tractatus de Variolis, & Morbillis, &
Epiſtola eiuſdem Auct. dè Prauis Febribus cum peticulis, quæ anno MDXC. & XCI. per Italiam vagarunt.

AD SERENISSIMAM D CHRISTIANAM LOTHARINGIAM MAGNAM ETRVRIÆ DVCISSAM.

FLORENTIAE,
APVD PHILIPPVM IVNCTAM. MDXCIII.
Cum Licentia Superiorum, & Priuilegio.

Title page of Trunconius' book.

Et papulae turpi sanie crebroque fluentes,
Et terrae subito allidens ἐπιλησία corpus;
Motibus ac tremulis quatiens convulsio membra,
Et teneris saniosae haerentes faucibus aphthae,
Quique gravi laniant lumbrici viscera morsu,
Tonsillae βάτραχος singultus, nausea, tussis,
Strumae, intertrigo, vesicae calculus, alvi
Profluvium et geminos circum foeda hernia testes,
Σειρίασις vomitus, alia et sexcenta malorum
Portenta heu nimium teneris infesta puellis,
Quae tua, Trunconi, haec cunctos monumenta per annos
Victura ostendunt tuto removere, parata
Unde tibi aeternum tanta est jam gloria, nullis
Terrarum trifidive coercita finibus orbis.

To thee, who dost on famous scroll indite
The child-bed goddess Juno's solemn rite,
Learned Trunconius, every sire who bears,
For child or grandchild, pledges sweet, his cares,
Nor less the matron, she no novice wed,
Pays honour, for that in thy book well read
She learns to bear the toils of motherhood;
They too whose skill it is with effort rude
The limbs to drag through gaping frame of bone
Give praise; but most is bound to thee, Truncon,
The host of infants struggling to the birth,
For that thou spread'st for them the way to earth,
Making it easy from their prison cell;
Thou too dost keep them in sound health and well,
To green old age and goodly length of life,
Rescued from danger, from each plague that's rife,
Which doth their tender frame attack, and these
From wasting savest, and from foul disease,
From ὑδροκέφαλος with its vast head,
From scabs and running sores unsightly bred,
From ἐπιλησία which sudden fells
To earth, and from the shaking limb that tells
Of strange convulsion, and the aphthous sore
That clings about the tender throat, and more,
The worm whose bite the inward part doth tear,
Frog-throated βάτραχος and nausea,
Hiccup and cough, and swollen glands, and stone,
And intertrigo, nor these ills alone
But flux of bowel, and each groin below
Distressful hernia, and fevered glow
Of Σειρίασις vomiting and all
The thousand wondrous ills that may befall
Frail childhood, these thy monumental scroll,
Destined to last as long as years shall roll,
Has safely banished. For this book of thine,
Trunconius, on thee shall glory shine
For ever and for ever, and its bounds shall be
Unchecked by bounds of earth or sky or sea.

Pediatrics in Art

INFANTILE ALCOHOLISM

JOHN RUHRÄH, M.D.
BALTIMORE

Guido Reni (1575-1642) of Calvanzàas, near Bologna, contributes an interesting picture relating to infantile alcoholism, a subject of interest today owing to prohibition. His "Little Bacchus" in the Dresden

Der kleine Bacchus.

Gallery illustrates several of the symptoms produced by alcohol—drowsiness, carelessness and the easy influence of suggestion as evidenced by the urination induced by the sound of the running wine. As Shakespeare has it in Macbeth, the Porter answers Macduff's question: "What three things does drink especially provoke?" "Marry Sir, nose painting, sleep and urine." The photograph is by Königliche Gemälde Gallerie, Dresden.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

Irregular Ossification of the Extremities of Boys and Girls. Ruth Otis Sawtell, Am. J. Roentgenol. **25**:330 (March) 1931.

Three groups of children from private schools in different parts of the country were studied, i. e., from New York, Iowa and Michigan. Irregularities in the ossification of the extremities appear frequently on the roentgenograms of the so-called normal child. They are of two types, supernumerary centers and double epiphyses, and proximal epiphyses when only distal epiphyses are expected. Both kinds are more common in the foot than in the hand, but disappear there more quickly because of a more rapid rate of ossification. The incidence is higher in men than in women, and union and disappearance are slower; this is in accord with the normal sex difference in ossification.

Stulik, Chicago.

Comparative Study of the Antibody Response After Various Methods of Administration of Mixed Typhoid Vaccine, with Particular Reference to the Intradermal and Oral Methods. Louis Tuft, J. Infect. Dis. **50**:98 (Feb.) 1932.

Agglutinins against typhoid are highest in concentration about six weeks after an initial injection of vaccine. The authors did not find any comparison between complement-fixing antibodies and agglutinins. In fact, with very high dilutions there were at times no complement-fixing antibodies. They likewise were not able to confirm the observations of other investigators that oral vaccine was of any value.

Toomey, Cleveland.

Immunity to Vaccination Produced in Rabbits by the Repeated Injection of a Testicular Vaccine Virus Filtered Through a Basic Filter. S. P. Kramer, J. Infect. Dis. **50**:119 (Feb.) 1932.

Filtrates of testicular vaccine virus may immunize rabbits against vaccinia.

Toomey, Cleveland.

Derivation of Staphylococcus Albus, Citreus and Roseus from Staphylococcus Aureus. Max Pinner and Marie Voldrich, J. Infect. Dis. **50**:185 (March) 1932.

In the experiments of these authors, it was shown that the three nonpathogenic strains of albus, citreus and roseus may be split off from pure line strains of pathogenic Staphylococcus aureus. The authors also were able to reverse their process, and produced aureus from albus strains.

Toomey, Cleveland.

The Effect of Urine on Hemolytic Streptococci. G. H. Robinson and F. A. Taylor, J. Infect. Dis. **50**:249 (March) 1932.

Urine inhibits the growth of hemolytic streptococci, while other indifferent streptococci grow abundantly in it. Urine in itself is not a streptococcic dissociant.

Toomey, Cleveland.

THE TOXICITY OF IODINE FOR THE CELLS OF MYCOBACTERIUM TUBERCULOSIS. G. KNAYSI, J. Infect. Dis. **50**:255 (March) 1932.

Iodine is toxic to the tubercle bacillus even in such low dilutions as 1:10, since organisms treated with a solution of the latter strength for thirty minutes did not grow on slants, and exposure for fifteen minutes prevented the infection of guinea-pigs.

TOOMEY, Cleveland.

THE USE OF IODINE AND CERTAIN IODINE COMPOUNDS IN EXPERIMENTAL TUBERCULOSIS. G. KNAYSI, J. Infect. Dis. **50**:261 (March) 1932.

Iodine is useless from a therapeutic standpoint, since it did not bring about any clinical improvement in the tuberculosis of rabbits into which injection with the material had been made.

TOOMEY, Cleveland.

THE INFLUENCE OF BLOOD AND OF EXUDATE ON THE ACTION OF BACTERIOPHAGE AGAINST THE COLON BACILLUS. MARTHA APPLEBAUM and WARD J. MACNEAL, J. Infect. Dis. **50**:269 (March) 1932.

Purulent exudate, pus, blood or serum may interfere with the toxicity of bacteriophage.

TOOMEY, Cleveland.

THE RESPIRATORY FLORA OF ESKIMOS IN REMOTE NORTHERN REGIONS. J. RALPH WELLS and PETER HEINBECKER, J. Infect. Dis. **50**:281 (April) 1932.

The respiratory flora of Eskimos in remote Arctic regions are similar to the flora of persons living elsewhere. The most common organism found was the staphylococcus, often of hemolytic character, and next in the order of frequency of occurrence were: gram-negative diplococci, Streptococcus viridans, diphtheria-like bacilli, Sarcinae, Micrococcus pharyngis-siccus, colon bacilli, gram-positive cocci, indifferent streptococci, Micrococcus catarrhalis, Micrococcus tetragenus, Streptococcus hemolyticus, Friedländer's bacillus, Streptothrix and yeasts.

TOOMEY, Cleveland.

BILIRUBINEMIA IN CHILDREN UNDER PHYSIOLOGIC CONDITIONS. P. GORINI, Riv. di clin. pediat. **30**:368 (March) 1932.

The author studied a series of cases for the presence of bilirubin in the blood, using the van den Bergh test. There were twelve breast-fed children, twelve artificially fed children under 1 year of age and eight children between 1 and 2 years of age, none of whom had disease of the biliary tract.

In none of these cases was bilirubin found in the blood. The author concludes that the existence of bile pigment in the blood is always pathologic and is probably due to dysfunction of the liver.

HIGGINS, Boston.

FURTHER INVESTIGATIONS OF THE ACTION OF CERTAIN STEROLS AND OF ULTRAVIOLET RAYS ON WHITE MICE. C. W. HERLITZ, I. JUNDELL and F. WAHLGREN, Acta pædiat. **12**:221, 1932.

The authors had previously observed cardiac lesions in white mice and other animals treated for a long period with cod liver oil, with inactive and activated viosterol and with egg yolk. Addition of chemically pure cholesterol, 1 Gm. a day per animal, to the stock diet produced no cardiovascular lesions, nor did pure viosterol in a dosage of 0.1 mg. a day per animal.

Previous investigations had also shown that in mice receiving roentgen rays for one hour a day at a lamp distance of 70 cm. for about two hundred days, commencing at 15 days of age, malignant neoplasms of the dermis of the ears and tail similar to those evoked by painting with crude coal tar developed. These

animals also showed in frequent instances—in fact, in virtually every case in which there was pronounced formation of tumor—cardiac lesions identical with those previously described, comprising degenerative changes, atrophy, destruction of heart muscle cells and proliferative changes in the interstitial tissue, often with deposition of calcium salts. Focal necroses of the liver, associated with small erythrocyte emboli, were not uncommon. Similar changes were brought about in animals that received direct ultra-violet rays as well as the addition of pure cholesterol to the stock diet. In the control series, 36 per cent of the animals showed cardiac lesions of similar nature but of lesser degree. Thus the relation of these cardiac lesions to antirachitic therapy remains obscure.

Excellent photomicrographs are reproduced.

McINTOSH, New York.

DEPENDENCE OF NORMAL RENAL FUNCTION ON THE SIZE OF THE BODY. C. HOLTEN, Acta pædiat. **12**:251, 1932.

Previous investigators had shown that the weight of the kidneys bears a fairly constant ratio to the surface area of the body. The maximum amount of blood plasma that can be cleared of urea by renal activity in unit time (Van Slyke's "maximum clearance") also bears a constant relation to the weight of the kidneys and therefore also to the surface area of the body.

Rehberg has studied creatinine excretion similarly, and one may express maximum creatinine clearance for unit time by the formula

$$\frac{\text{(Per cent of urinary creatinine)} \times \text{(urine volume)}.}{\text{(Per cent of blood creatinine)}}$$

The author made creatinine determinations in ninety children from 9 months to 17 years of age, under conditions of moderate diuresis; calculating the amount of glomerular filtrate (or creatinine-cleared plasma) by Rehberg's formula, he compared this value with observations of body weight and of surface area calculated by the Du Bois formula. The correlation of renal function as determined by this test and surface area is conspicuously close at all ages. It is inferred that renal function in the foregoing sense and basal metabolism run parallel.

The average glomerular filtrate for one square meter of surface area per minute is 83 cc.; an output of less than 60 cc. should be regarded as pathologic.

McINTOSH, New York.

Nutrition

THE RELATION OF BLOOD SUGAR TO BLOOD VOLUME AND CARBOHYDRATE TO WATER RETENTION. J. F. McCLENDON, Am. J. Physiol. **98**:216 (Sept.) 1931.

In experiments on normal men who were fasting, the drinking of water resulted in only small changes in blood sugar and blood volume, and all the water was excreted in a few hours. Taking dextrose with the water (400 Gm. of dextrose in 2,400 Gm. of water in eight hours) resulted in a marked increase in volume of blood and retention of water, and an increase of about 1 Kg. in body weight.

NOURSE, Cleveland.

THE EFFECT OF A DIET OF POLISHED RICE ON THE MINERAL CONTENT OF THE CARCASSES OF PIGEONS. J. S. McHARGUE and W. R. ROY, Am. J. Physiol. **99**:221 (Dec.) 1931.

The ash from the carcasses of pigeons fed polished rice until polyneuritis developed showed a marked diminution in magnesium, phosphorus and potassium content, as well as in the content of some of the minor constituents. Recovery followed the feeding of unpolished rice, wheat and yellow corn. Following recovery, the mineral content of the ash approached the normal level, but still remained below that of the normal controls.

NOURSE, Cleveland.

EXOPHTHALMOS IN INFANTILE SCURVY. J. H. DUNNINGTON, Arch. Ophth. **6**:731 (Nov.) 1931.

Because of the paucity of detailed reports of exophthalmos in infantile scurvy, the author records his observations. It is often stated that exophthalmos occurs in 10 per cent of the cases. This figure is too high—2 per cent being nearer the truth. The direction of the proptosis is constant, being forward, downward and outward. Many authors contend that hemorrhage, which is the causative factor, occurs in the areolar tissue of the orbit, while the presence of blood beneath the periosteum of the orbital plate of the frontal bone has been demonstrated as the site of the hemorrhage. The hemic origin of the proptosis accounts for the position of the eye, the sudden appearance of the proptosis and its proneness to recur if not treated. If antiscorbutic treatment is instituted promptly, the protrusion disappears in from four days to four weeks. The variations in degree of proptosis are marked in any series of cases, being so severe at times as seriously to endanger the cornea. The exophthalmos is nonpulsatile, and any attempt at reduction causes pain and may cause a recurrence of the hemorrhage or proptosis. The condition is usually bilateral, but not simultaneously so, and one eye is more exophthalmic than its fellow. The left eye is more frequently involved than the right. While scurvy is a disease of all ages, exophthalmos as a complication is found most frequently in children under 2 years.

WESCOTT, Chicago.

THE NUTRITION OF SICK CHILDREN. M. G. PETERMAN, IRMA HUG and NELL C. CLAUSEN, Arch Pediat. **49**:67 (Feb.) 1932.

This is the continuation of an investigation reported in August, 1930, to determine the food requirements of children sick in the hospital with chronic diseases, particularly tuberculous bone lesions. The study is especially concerned with the effect of high fat, acid ash and base ash diets, and the influence of sodium chloride. The author states: "We may restate our previous conclusions that the food requirements of tuberculous children should exceed by 50 per cent the basal requirement calculated on the basis of the "normal" or expected average weight. These requirements are approximately those for normal, well, active children. They are best supplied in concentrated food. From these studies, under the stated conditions, the ideal diet for children with bone tuberculosis was a basic ash, high vitamin, high mineral, attractive diet. The sodium chloride allowance was not an important factor.

"The object of this paper is to present data obtained from a group of children with tuberculous bone disease, under the average or usual care, which might be of value in establishing standards for comparison and for further study."

WADDELL, University, Va.

RACHITIC OSTEOMALACIA: REPORT OF A CASE TREATED BY MASSIVE DOSES OF VIOSTEROL. MAURICE L. BLATT and LIONEL B. SAFFRO, Arch. Pediat. **49**:109 (Feb.) 1932.

A case of rachitic osteomalacia occurring in a Negro boy 5 years old is reported. Treatment consisted of massive doses of viosterol. The equivalent of 210,700 drops of viosterol (250 D) was used between Jan. 23, 1931, and May 3, 1931, a period of one hundred days. A maximum daily dose of 6,400 drops was given for a period of twenty-one days. There was no evidence of toxicity, and massive doses of viosterol favorably influenced the blood calcium, phosphorus quotient and bone calcification. Although good results were obtained in the reported case, the writers do not recommend the use of such massive doses.

WADDELL, University, Va.

VITAMIN-B AND VITAMIN-G CONTENT OF CEREALS. ROSSLEENE ARNOLD HETLER, CLARA ROCKE MEYER and DOROTHY HUSSEMAN, Illinois Agric. Exper. Sta. Bull., no. 369, 1931, p. 167.

The vitamin B and vitamin G values of oats and oat products, corn, wheat, rice polishings and tikitiki were studied by determination of the rate of growth of albino rats when the cereal or cereal product furnished the sole source of these vitamins in the diet. Both vitamins B and G were present in the cereals and cereal products studied. Vitamin G is the limiting factor of the vitamin B complex of cereals. A diet including 50 per cent of any of the cereals supplied enough of the heat-stable vitamin G for approximately normal growth, while 25 per cent of any of the cereals provided enough vitamin B. Vitamin G is present in tikitiki. When a diet containing Crisco and corn starch instead of dextrose was used for the vitamin B tests, a somewhat higher amount of any of the cereals was necessary to furnish sufficient vitamin B for good growth.

KUGELMASS, New York.

THE NUTRITIVE VALUE OF CEREALS AND ITS RELATION TO PROCESSING. THOMAS B. PARKS, Iowa State Coll. J. Sc. **5**:349, 1931.

For all foods investigated the proportion necessary for satisfactory growth was less than for reproduction, and reproduction required smaller proportions than lactation. Vitamins B and G are the factors that are effective. From 8 to 20 per cent of white wheat, scoured white wheat and Pettijohn's breakfast food sufficed as the sole source of vitamins B and G for normal growth but not for reproduction. Growth was better on a diet of cleaned durum wheat than on pearled durum wheat. Puffing wheat seems to destroy vitamins B and G. Whole oats and rolled oats are inferior to wheat as a source of vitamins B and G, but cleaned oats, dried oats, oat groats and rolled oats are as good as whole oats. Oat hulls were better sources of vitamin B and G than the oats. Rolled oats, milk or cream, sugar and salt were satisfactory for reproduction. The rats chose 28 per cent rolled oats and 72 per cent milk when given their choice. This ration produced especially vigorous animals.

KUGELMASS, New York.

REPRODUCTION AND LACTATION ON SIMPLIFIED DIETS. MILTON W. TAYLOR, Iowa State Coll. J. Sc. **5**:355, 1931.

Cod liver oil was found to contain vitamin E. Petroleum or mineral oil prevented reproduction even when wheat germ oil was included in the diet. Crude can molasses and sorghum contained vitamin D. The fertility of males is affected much more by restricted diets than is that of females. Both vitamins A and E are destroyed by ferrous chloride. Vitamin G was shown to be the limiting factor in these diets.

KUGELMASS, New York.

RELATIONSHIP OF VITAMIN A TO RESPIRATORY INFECTIONS IN INFANTS. L. H. BARENBERG and J. M. LEWIS, J. A. M. A. **98**:199 (Jan. 16) 1932.

An investigation to ascertain whether or not a diet deficient in vitamin A was related to the incidence of respiratory infections failed to reveal any relationship.

BONAR, Salt Lake City.

THE INFLUENCE OF THE CANNING INDUSTRY IN THE CHANGING DIETARY. E. F. KOHLMAN, J. Am. Dietet. A. **6**:123 (Sept.) 1930.

The author makes the point that loss of food value in open kettle-cooked foods is due to the loss of vitamin content by oxidation. Properly canned foods have the following advantages over home-cooked storage foods: 1. Oxygen is

effectively removed and vitamins are preserved. 2. Foods are canned fresh and ripe at harvest time. 3. Iodine-containing foods, such as salt water fish, may be transported to areas where the soil is poor in this mineral.

PARKER, Rochester, N. Y.

EFFECT OF PROLONGED USE OF AN EXCLUSIVE MEAT DIET. WALTER S. MCCLELLAN, J. Am. Dietet. A. **6**:216 (Dec.) 1930.

V. Stefanson and K. Anderson, arctic explorers, lived exclusively on a meat diet for one year. Approximately 25 per cent of calories were furnished by protein and 75 per cent by fat, the amounts of fat and protein being varied independently. The following observations were made: 1. When 40 per cent of calories were supplied by protein, digestive disturbances occurred, and it was difficult to satisfy the appetite. 2. When over 80 per cent of calories were supplied by fat, the subject became more and more drowsy, with an increase of ketosis. 3. Mild ketosis persisted throughout the year. 4. No signs of injury to the kidneys occurred in spite of the high protein intake. 5. The tolerance for carbohydrates was definitely lowered temporarily. 6. The subjects remained in nitrogen balance except during attacks of pneumonia, when a marked negative balance occurred. 7. There was a marked negative calcium balance. 8. There was no evidence of storage of nitrogen in the body in spite of the extremely high intake of protein.

PARKER, Rochester, N. Y.

"BREAST FEEDING." JACK F. PERKINS, Texas State J. Med. **27**:808 (March) 1932.

An earnest plea is made to feed the majority of infants from birth to between 6 and 9 months on breast milk. Various excuses often given by the mother and the physician are mentioned and refuted by the author. It is suggested that the physician caring for the breast-fed infant regulate the diet of the lactating mother, emphasizing the value of minerals and vitamins advantageous to the well-being of the offspring.

MOORE, Dallas, Texas.

MILK INTOLERANCE AND ALEURONE OF SUNFLOWER. R. A. MARQUÉZY, Bull. Soc. de pédiat. de Paris **29**:375 (July) 1931.

The cases of a number of infants who did not digest milk well are cited. They had persistent diarrhea, with curds and mucus in the stools. They were fed a mixture consisting of sunflower, 4 per cent, cream of rice, 10 per cent, sodium chloride, 0.10 per cent, malt syrup, some brewer's yeast (for vitamin B), cod liver oil (for vitamin A) and fruit juice (for vitamin C). The infants took the mixture well, and the stools improved rapidly, in some cases after the patients were on the feeding for only twenty-four hours. Gradually they were all given a mixture of dry milk, which they took without any trouble and thrived on. The author considers that these infants are suffering from a milk intolerance and believes that a milk-free feeding until the diarrhea ceases is the treatment indicated.

BENJAMIN, Montreal, Canada.

INFLUENCE OF THE ALKALINE RESERVE ON THE CALCIUM AND POTASSIUM CONTENT OF THE SERUM. D. BROUN and J. STOYANOVA, Compt. rend. Soc. de biol. **107**:1511 (Sept. 18) 1931.

Fisher has shown that hypnotics produce variation in the calcium and potassium content of the serum; that they are increased in alkalosis and decreased in acidosis. The action of hypnotics is likewise modified by alkaline and acidotic states.

The author studied, therefore, the variations of the calcium and potassium content of the blood serum in dogs having these conditions. Acidosis was pro-

duced by intravenous injections of lactic acid, and alkalosis by sodium bicarbonate. In acidotic dogs, there is produced an increase of from 2 to 37 per cent in the calcium content; the potassium, especially the fixed portion, is decidedly diminished. In experimental alkalosis the calcium was definitely diminished, especially the fixed portion (33 to 62 per cent); the potassium content was increased 20 per cent.

Therefore, in the dog, a diminution in the reserve of alkaline leading to an experimental acidosis increases the calcium and diminishes the potassium. Inversely, an increase in the reserve of alkaline produced by experimental alkalosis led to a diminution in the serum calcium and an increase in the potassium. Calcium and potassium vary in an opposite way, being liberated from tissues to which they are fixed.

WAHL, Cleveland.

THE INFLUENCE OF VIOSTEROL ON THE CALLUS FORMATION IN FRACTURES. JEAN MORRELLE, Compt. rend. Soc. de biol. **108**:803 (Nov. 27) 1931.

The fibulae of old and young rats were fractured. Three series were studied: one, a control group; two, a group receiving small doses and, third, a group receiving large doses of standardized viosterol.

The healing process of the fracture was compared for the amount of callus formation, as shown in the roentgenograms taken at frequent intervals. Morrelle was convinced that the fractures in the young and adult rats alike healed more rapidly with small doses of viosterol, and that healing was definitely delayed in rats treated with large doses, as compared with those receiving normal doses or those that were untreated.

WAHL, Cleveland.

CARDIAC BERIBERI OF THE NURSLING. J. ALBERT, J. hyg. soc. **60**:1008, 1931.

Infantile beriberi is responsible for 28 per cent of deaths of infants under 1 year of age in the Philippines. Of the three forms (aphonic, pseudomeningitic and cardiac) the latter is the most serious. At autopsy there are cardiac hypertrophy and dilatation (often only of the right side of the heart), diffuse congestion of the viscera and anasarca. A degenerative neuritis of the vagus occurs with long duration of the disease. The malady is observed always in an infant between 1 and 3 months of age, nourished by a mother suffering from latent or "partially apparent" beriberi. The infant is generally well developed, often large, and considered in good health.

THATCHER, Little Rock, Ark. [ARCH. PATH.]

THE FUNDAMENTAL PRINCIPLES OF METABOLISM. H. BOHNENKAMP and W. PASQUAY, Arch. f. d. ges. Physiol. **228**:40, 1931.

In this series of five papers a study is made of the physical principles involved in the total loss of heat. This total loss of heat occurs by radiation, conduction and convection, and in vaporization of the insensible perspiration. The latter process has been shown by Benedict and Root to have a linear relationship to the total exchange of energy and can be expressed in terms of the other quantities. The loss by conduction and convection can be assumed to be 100 calories with a slight error. The loss by radiation is thus the determinative magnitude, and means for its estimation form the chief object of this series of studies.

By the Stefan-Boltzmann law, radiation from a dark body depends on its surface area and its surface temperature. In man the surface that radiates is not the total surface area, since some of the surfaces are apposed. The "effective surface" was measured by a photographic method, and the actual radiation was measured by a special instrument. A method was devised for rapid measurement of the electrical capacity of the subject from which the effective surface can be calculated. The effective surface, which was determined by this method in a large number of cases, is in general 85 per cent of the total surface as given by the height-weight formula of DuBois.

The surface temperature is taken as the mean skin temperature. This is the factor that is affected by sex, age and nutritional state. Since the mean value is involved, it is approached indirectly. It is related to the insulating layer of subcutaneous fat which in turn is proportional to the specific gravity of the person. The specific gravity was obtained from the weight and the net volume, the latter being measured by an air displacement method. Finally the mean skin temperature is calculated from the specific gravity.

This formulation is offered in place of the present more or less empiric one because it keeps the essential physical factors clearly in mind and also is more accurate for the prediction of metabolism than the present standard tables.

KISER, Atlanta, Ga.

METABOLIC DISTURBANCES IN PELLAGRA AND THEIR MODIFICATION BY INSULIN. O. KAUFFMAN-COSLA, C. PARHON-STEFANESCU and O. VASILCO, Deutsches Arch. f. klin. Med. **172**:145 (Dec. 8) 1931.

The authors review the theories of the pathogenesis of pellagra and summarize their own investigations as follows: 1. Patients with pellagra suffer a metabolic disturbance manifested as dysoxidative carbonuria. 2. Intermediate products of sugar metabolism (acetic aldehyde and lactic acid) are eliminated in increased quantities in the urine. 3. Insulin reduces this increased elimination of dysoxidative carbon. 4. The metabolic disturbance involves the carbohydrate group primarily. 5. The dysoxidative carbonuria and the effect of insulin on the general metabolic disturbance justify the assumption of a theory of avitaminosis in the etiology of pellagra.

DOOLEY, Kent, Conn.

THE RÔLE OF THE HEMATO-ENCEPHALIC BARRIER IN THE PATHOGENESIS OF THE NEUROTOXIC SYNDROME IN ACUTE NUTRITIONAL DISTURBANCES: VI. SUGAR OF THE BLOOD AND SPINAL FLUID. S. J. SCHAFERSTEIN, Jahrb. f. Kinderh. **134**:216 (Jan.) 1932.

The author found no hyperglycemia in toxic states. The mean ratio of the concentration of sugar in spinal fluid and in blood was found to be 0.65 in nontoxic states, and 0.78 in toxic states; in certain toxic cases the ratio approached unity.

CLAUSEN, Rochester, N. Y.

CHANGES IN POTENTIAL-DIFFERENCE IN CHILDREN UNDER DIFFERENT CONDITIONS. P. MEDOWIKOV, H. DERNOWA, E. LEBEDOWA and A. MARENINA, Ztschr. f. Kinderh. **52**:331 (Feb. 9) 1932.

The electric potential-difference was measured by means of the Strauss galvanometric method in 102 children during varying periods of the day and season of the year, and also after sunbathing. There was a great variation in different children, although there was a definite tendency toward a higher potential-difference in sympathicotropic than in vagotropic children. The variations in potential-difference may be due to changes in the colloidal state of the organism.

SHELLING, Baltimore.

THE EFFECT OF THE TOXIC COMPONENT OF IRRADIATED ERGOSTEROL ON PHOSPHATASE OF THE BONE. G. BISCHOFF and A. LOESCHKE, Ztschr. f. Kinderh. **52**:349 (Feb. 9) 1932.

Bone phosphatase was determined in rachitic dogs given large doses of irradiated ergosterol containing the toxic factor. It was found that rachitic dogs are less susceptible to the "toxic factor" than are normal dogs, and that it decreases the bone phosphatase in both normal and rachitic animals.

SHELLING, Baltimore.

THE EFFECT OF LARGE DOSES OF CREATINE ON THE EXCRETION OF PHOSPHORIC ACID IN THE URINE. H. FOSOLD and A. LOESCHKE, Ztschr. f. Kinderh. **52**:358 (Feb. 9) 1932.

Previously it was shown by Brown and Imrie that large doses of creatine will depress the urinary excretion of phosphorus in animals. The retained phosphorus was thought to be stored in the body with the retained creatine as phosphogen. Since Beumer has shown that children below the age of puberty do not utilize exogenous creatine, it would follow that the administration of creatine to children should not depress the phosphorus excretion in the urine. In repeating the experiments on children and on themselves the authors found that in children creatine produces no effect on the urinary phosphorus; and that the changes in the urine of adults need not necessarily be due to formation of phosphogen, since the large amounts of water given with the creatine may produce similar effects.

SHELLING, Baltimore.

THE ANTIRACHITIC VITAMIN FROM VIOSTEROL. A. WINDAUS and A. LÜTTRINGHAUS, Ztschr. f. physiol. Chem. **203**:70, 1931.

Now that the vitamin D has been separated from the irradiation products of viosterol into two definite crystalline substances, D_1 and D_2, and now that the physical and physiologic properties of these have been definitely determined, various hypotheses of other investigators are disposed of. Among these are Gerlach's view that viosterol in an "excited" state functions as an antirachitic vitamin, Takayima's assertion that vitamin D is an ozonide of viosterol, Castille's assumption that the vitamin is an epimeric form of viosterol and Jendrassik's claim that irradiation destroys the power of viosterol to absorb ultraviolet rays. The toxicity resulting from excessive doses is an actual property of the vitamins. The "new calciferol" recently reported by Askew and others is shown to be identical with D_2. By means of the dinitrobenzoic ester separation, D_1 has just been found to consist of a constant mixture of D_2 and an isomeric alcohol.

KUGELMASS, New York.

Prenatal Conditions

THYROGLOSSAL DUCT CYST AND SINUS. PAUL O. SNOKE, Am. J. Roentgenol. **24**:424 (Oct.) 1930.

A case of thyroglossal duct sinus is presented in which the lateral anlage ducts are believed to have persisted rather than the usual median duct. Roentgen demonstration was made possible by the use of a ureteral catheter and iodized oil. This case disproves the generally accepted idea that only midline sinuses are due to thyroglossal duct remnants.

STULIK, Chicago.

PROPHYLAXIS OF THE ANEMIA OF PREMATURE INFANTS. ARTHUR F. ABT and BETH R. NAGEL, J. A. M. A. **98**:2270 (June 25) 1932.

Various therapeutic agents have been of questionable value in the cure of anemia of premature infants. Adequate prophylaxis has not been attempted. The authors found iron therapy alone of doubtful value, while desiccated hog's stomach and the use of liver fraction alone fared a similar fate. The latter combined with ferrous ammonium citrate seemed to give favorable results when started within the first two weeks after birth in initial doses of from 1 to 2 Gm. daily. The dose was increased to 4 Gm. twice daily. The best response was in the group from 6 to 7 months of gestational age with marked anemia. Regarding the etiology, the authors favor the view that the anemia is due to functional insufficiency of an imperfectly developed hematopoietic system.

BONAR, Salt Lake City.

CONGENITAL PROTEIN HYPERSENSITIVENESS: PROTEIN HYPERSENSITIVENESS TRANSMITTED FROM ALLERGIC MOTHER TO CHILD. BRET RATNER and JANET E. GREENBURGH, J. Allergy **3**:149 (Jan.) 1932.

Protocols are given of two families in which the mother and one of her children were hypersensitive to protein.

The child may become passively sensitized by the transmission of antibodies of substances to which the mother is sensitive or actively sensitized by the passage through the placenta of antigens ingested by the mother during the latter months of pregnancy. Placental filtration of antibodies and antigens is a mode of inheritance that is not germinal or chromosomal, and the manner of sensitization does not differ from the sensitization acquired by inhalation, ingestion or injection of sensitizing substances.

Guinea-pigs into which serum from a mother sensitive to horse dander was injected developed definite anaphylactic reaction on receiving a shocking dose of horse dander. This would tend to show that allergic antibodies and anaphylactic antibodies are identical.

The authors feel that congenital hypersensitiveness to protein is a definite type of sensitization, but do not deny that there is still the unknown quality of susceptibility, the how and why of which still is not clear.

HOYER, Cincinnati.

EIGHT CASES OF CONGENITAL HEART DISEASE. WILLIAM T. READ, JR., and E. B. KRUMBHAAR, M. Clin. North America **16**:229 (July) 1932.

Probably the most common cardiac anomaly is pulmonary stenosis. When this is accompanied by an interventricular septal defect together with partial transposition of the aorta and hypertrophy of the right ventricle, it is known as the tetralogy of Fallot. The histories of three such cases with postmortem observations are reported. The duration of life in this type of case depends on the degree of pulmonary stenosis. It varied in the cases reported from two days to five years. Two cases of complete transposition of the great vessels are described. In this condition, two separate circulations are maintained, and during fetal life oxygenation of the blood in the general circulation is accomplished during its passage through the placenta. After cessation of the placental circulation, however, oxygenated blood can get into the systemic circulation only through the ductus arteriosus, the foramen ovale, a septal defect or an anomalous extracardiac vessel. In one of the cases reported in which the patient lived eleven days, an anomalous vein from the left auricle presumably carried some aerated blood to the superior vena cava. Two cases of anomalous semilunar cusps, one with coarctation of the aorta and one of premature closure of the foramen ovale, are described. The patient with coarctation of the aorta lived a fairly normal existence for thirty-five years owing to the establishment of a marked compensatory collateral circulation in the internal mammary arteries.

SMITH, Ogden, Utah.

MICROCEPHALY. E. A. WHITNEY, M. J. & Rec. **135**:166 (Feb. 17) 1932.

The author considers microcephaly one of the most fascinating subdivisions of craniology. He points out that microcephaly is noted in the earliest writings, sculptures and drawings of mankind. Particularly is this true of Egyptian and Aztec sculptures and drawings. According to Castelli, in certain tribes of central Asia the condition is so common that the natives look on it as natural. The etiology, characteristics and mental and physical development are then discussed. A full description of the brain found in microcephalic persons is then given in the paper. The tendency toward familial microcephaly has often been pointed out in the literature.

WILLIAMSON, New Orleans.

SPONTANEOUS CURE OF SPINA BIFIDA WITH CONGENITAL DISLOCATION OF THE LUMBAR SPINE. DAVID KYLE, Brit. M. J. **1**:1076 (June 11) 1932.

The case reported is one of spina bifida diagnosed at birth. At 12 years of age, the roentgen and other findings showed evidence of complete cure of the spina bifida but permanent dislocation of the lumbar spine.

ROYSTER, University, Va.

PARTIAL HEMIHYPERTROPHY. W. CAMERON-DAVIDSON, Proc. Roy. Soc. Med. **24**:1340 (Aug.) 1931.

This case showed, in a girl of 5 years, marked hypertrophy of the right leg and slight hypertrophy of the right arm and hand and of the right side of the face. The patient also showed the fine nevoid condition of the skin and, to a slight degree, the mental deficiency associated with this condition. All ligaments and muscles were lacking in tone, and a kyphosis was present. There was flaccidity of abdominal muscles noticed particularly in coughing.

WILLIAMSON, New Orleans.

1. GIGANTISM (ACROMEGALIC IN TYPE). 2. A MIDGET. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **24**:1352 (Aug.) 1931.

These two cases were reported in girls aged 8 and 7 years respectively. The report is accompanied by photographs of the patients.

WILLIAMSON, New Orleans.

RIGHT DIAPHRAGMATIC HERNIA. DONALD PATERSON, Proc. Roy. Soc. Med. **25**:139 (Dec.) 1931.

A case of right diaphragmatic hernia is reported in a girl aged 10 months.

WILLIAMSON, New Orleans.

RIGHT-SIDED DIAPHRAGMATIC HERNIA. HUGH THURSFIELD, Proc. Roy. Soc. Med. **25**:783 (April) 1932.

A boy, aged 16 months (one of twins), was admitted to the hospital because of vomiting and general backwardness in development. He had always been thin and had once vomited altered blood. His weight was 14 pounds (6.4 Kg.) on admission, and he was pale and rickety. He did not walk or talk, and his heart was displaced to the left. Examination immediately after a barium meal showed an hour-glass stomach, the upper part being above the right dome of the diaphragm, and twenty-four hours afterward, a loop of colon was seen in the thorax to the right of the esophagus.

The article is accompanied by pictures of the stomach after the barium meal.

WILLIAMSON, New Orleans.

THE CAUSE OF DEATH OF PREMATURE INFANTS. HANS KREUTZFELDT and ALBRECHT PEIPER, Monatschr. f. Kinderh. **52**:24 (Feb.) 1932.

This article details a clinical and pathologic study, with excellent illustrations. Careful investigation of the brains of seven infants born prematurely revealed hemorrhage into the pons as the cause of only one death. These observations are in contrast to those of Ylppö and others, who expressed the belief that the respiratory disturbances and death of premature infants are due to the hemorrhages around the respiratory centers. The authors conclude from their studies that the death of premature children accompanied with respiratory difficulty is simply due to the lack of development of the respiratory center.

GERSTLEY, Chicago.

COLON BACILLI IN THE STOMACHS OF PREMATURE CHILDREN. SUSANNE SEYFFARTH, Monatschr. f. Kinderh. **52**:73 (Feb.) 1932.

In nine prematurely born infants fed exclusively with breast milk, colon bacilli were found frequently in the stomach contents. While these children were in good health, their clinical course was in general less favorable than that of children not showing the colon bacilli. The children with positive findings often showed no diarrhea, but seemed to be the ones in whom diarrhea developed most readily following parenteral infection or change of diet. The slightest change of food, such as the addition of a small amount of cow's milk to the breast milk, was sufficient to lead to the development of colon bacilli in the stomach.

The bifidus flora did not become predominant until from the third to the fourth week. The writer believes that this is due to the relatively small quantity of breast milk taken during this time.

The author notes some relationship between disturbance of the bifidus flora, the development of the colon bacilli in the stomach and the appearance of thrush in the mouth.

GERSTLEY, Chicago.

THE PHYSIOLOGY OF THE PLACENTA: THE MANNER IN WHICH FAT PASSES THE PLACENTA. WERNER VON BICKENBACH and HANS RUPP, Ztschr. f. Geburtsh. u. Gynäk. **100**:1, 1931.

Up to the present time it has been the general contention that fat can go through the placenta only after being split into fatty acid and glycerin. This theory was advanced by analogy to the observations on the intestine, but has not been proved by incontestable experiments. The authors investigated this matter to ascertain whether or not certain kinds of fat could be found in the blood of the fetus after being injected into the blood of the mother. They chose types of fat that could be easily distinguished from normal blood fat that could be split by the lipase of the placenta, but could not be rebuilt by the organism. If afterward, only the normal fat could be found in the fetal blood and not the peculiar kind injected into the mother, the fats could have been transmitted only after having been split into fatty acids and corresponding alcohol. On the other hand, if, in addition to the normal glycerin fat, the injected fats could be found in the fetal blood and organism, one could state that the injected fat must have passed without being split or previously changed.

The authors made their experiments on pregnant rabbits during the last trimester of pregnancy. They injected methyl or amylester of oleic and palmitic acid. Afterward they found the same fats in the fetal blood, so these fats must have passed the placenta unchanged. Thus it has been proved that the fat passes the placenta without being previously broken down.

ADAIR and SIEDENTOPF, Chicago.

THE PHYSIOLOGY OF THE PLACENTA: THE ORIGIN OF FETAL FAT. HANS VON RUPP and W. BICKENBACH, Ztschr. f. Geburtsh. u. Gynäk. **101**:*27*, 1932.

The authors made investigations regarding the origin of fat on the growing fetus.

There are two absolutely different opinions on this subject. Investigators who attempted histologic dyeing of the fat in the placenta believe that the fetus gets its fat from the mother. The fact that the placenta is permeable for fat is proved by Hofbauer and the authors themselves. Other authors believe, in contrast, that the fetus builds its own fat from carbohydrates. Both opinions are logical. To decide which opinion is correct, the authors made the following experiment on nutrition: They fed rabbits, before and during pregnancy, a certain kind of fat which was easy to detect on account of its peculiar iodine number. They chose linseed, which contains linseed oil with an iodine number of 150-175. The normal fat of the rabbit has an iodine-number of 50-70. It is about the same in the

mother and fetus. The fat of the animals nourished with linseed, after a certain period of time, showed a definitely increased iodine number (120-140). When the iodine number of the fat in the fetuses of these animals was examined, it was found that their iodine number was increased also and equal to that of the mother.

Therefore this experiment proved that the fat of the fetus is of the same kind as that of the mother, and that the fetus gets its fat from the mother through the placenta.

ADAIR and SIEDENTOPF, Chicago.

INVESTIGATIONS ON ANIMALS REGARDING INTRA-UTERINE DAMAGE TO THE FETUS. PETER JONEN, Ztschr. f. Geburtsh. u. Gynäk. **101**:50, 1931.

The general opinion up to the present time has been that the fetus grows in utero, regardless of the nutritional condition of the mother, and that it deprives the maternal organism of whatever it needs. This theory was supported by observations made during the war, when undernourished mothers bore children of normal weight. The author made experiments on pregnant rabbits to see whether or not this theory was right in cases in which there was complete lack of nourishment. He made the following observations: When the mother was not fed, the fetus, in all cases, was ejected. In cases in which nourishment was withdrawn at the beginning of pregnancy, the embryo was decomposed entirely. The placenta also was either dissolved or ejected. If food was withdrawn at the middle of pregnancy, premature labor took place in all cases after from ten to twelve days. This happened before the mother had lost so much weight that she actually starved to death. Some of the animals lived for four days without any food after the miscarriage. A sufficient amount of glycogen and fat was found in the liver at the time of the miscarriage. The cause of the interruption of the pregnancy is not as yet clear. The lack of vitamins cannot be the only reason. The aborted fetuses were much smaller and of less weight than those of normally nourished mothers. The thymus gland and the bones showed marked changes. One must therefore conclude that the fetus cannot derive its needs from the maternal organism, regardless of the nutritional condition of the mother.

ADAIR and SIEDENTOPF, Chicago.

A SPORADIC CASE OF DYSOSTOSIS CLEIDOCRANIALIS. N. MALMBERG, Acta pædiat. **12**:291, 1932.

The case of a girl, aged 3½ years, showing dysostosis cleidocranialis, cervical and upper thoracic spina bifida and other malformations, is reported. The family history was unimportant.

McINTOSH, New York.

Diseases of the New-Born

THE EARLY TREATMENT OF INTRACRANIAL HEMORRHAGE IN THE NEW-BORN. I. NEWTON KUGELMASS, M. Clin. North America **15**:1313 (March) 1932.

Infants showing cyanosis or any respiratory disturbance should be placed in an oxygen tent or a Drinker box-respirator. Cisternal puncture is indicated immediately after birth in infants suffering from asphyxia or other conditions indicative of increased intracranial pressure. This may be repeated daily if necessary. Immediately after resuscitation, 15 cc. of whole blood should be injected into each buttock; the injection should be repeated daily until both clotting time and bleeding time have been reduced to five minutes. To combat shock and to supply fluid and nutriment, a solution of 3 per cent gelatin, 5 per cent dextrose and 0.5 per cent sodium chloride should be given every hour by a Breck feeder. The gelatin also serves to reduce the clotting time. After the second day a thick milk feeding, made up of 12 ounces (355 cc.) of evaporated milk, 18 ounces (532 cc.) of water and 3 ounces (89 cc.) of barley flour, may be given every four hours. All unnecessary handling must be avoided. Sodium

amytal, 1 grain (0.065 Gm.) in aqueous solution, or 1 ounce (30 cc.) of 1 per cent magnesium sulphate may be given by rectum when convulsions are not controlled by spinal drainage.

SMITH, Ogden, Utah.

EFFECT OF PRENATAL CARE ON THE INFANT. CLIFFORD G. GRULEE, Rep. Am. Child Health A. **6**:90, 1929.

The vast bulk of neonatal deaths is due to prematurity or congenital debility. Seven-eighths of the deaths occur from unknown causes or conditions that cannot be controlled and that cannot be affected by neonatal care. Of deaths occurring at term, common causes are malformation, hemorrhage, digestive troubles, icterus and syphilis. Of these, syphilis alone can be controlled.

The greatest help can be expected indirectly from the result of interest in conditions stimulated by neonatal care.

PARKER, Rochester, N. Y.

THE EFFECT OF INTRANATAL CARE UPON THE INFANT. W. R. RAMSEY, Rep. Am. Child Health A. **6**:99, 1929.

A contrast is drawn between intranatal care in Europe, where 85 per cent of children are delivered by midwives without intervention and with a low mortality, and this country, where 85 per cent of births are in the hands of physicians. Injuries and deaths are largely the result of the demand for painless, rapid births by instrument and anesthesia.

PARKER, Rochester, N. Y.

THE EFFECT OF POSTNATAL CARE ON THE INFANT. F. W. SCHLUTZ, Rep. Am. Child Health. A. **6**:106, 1929.

Mortality figures for the first two weeks of life have been little affected by care. The hope of reduction of mortality from injuries lies in improved obstetric training and diagnostic training of the practitioner. Second to prematurity, the greatest toll is taken by infection. The first two weeks are the period of greatest susceptibility. The common cold is the greatest offender. Wide thermal variations should be avoided. Adequate training of the practitioner in preventive pediatrics offers the greatest promise in the reduction of mortality.

PARKER, Rochester, N. Y.

RECOGNITION AND TREATMENT OF BIRTH INJURIES IN THE NEWLY BORN. G. B. FLEMING, Brit. M. J. **2**:481 (Sept. 12) 1931.

This article is a general survey of all injuries incident to birth drawn from the record of the Royal Maternity Hospital at Glasgow over a period of three and a half years. In this period eight thousand infants were born alive and among them were three hundred and fifty of more or less severe birth injuries. Each type of injury is discussed briefly. Special emphasis is placed on the intracranial hemorrhage group and the necessity for careful nursing of infants showing intracranial damage.

ROYSTER, University, Va.

B. COLI MENINGITIS IN THE NEW-BORN. JOHN GIBBENS, Lancet **1**:1298 (June 18), 1932.

Postmortem examinations on new-born infants during the past year at Queen Charlotte's Hospital revealed three cases of meningitis due to Bacillus coli.

The first patient, a girl, died on the eighteenth day of life, having shown a typical clinical picture of tetany. At postmortem examination the brain was found to be covered with a thick green layer of pus, thickest at the base; the right middle ear was also full of pus. Cultures from the meninges and the middle ear showed an almost pure growth of B. coli.

The second patient, also a girl, was at first thought to be suffering from intracranial hemorrhage. On the fourth day of life the fontanel became tense, and on lumbar puncture 1 cc. of thick pus was obtained. Postmortem and cultural observations were identical with those in case 1. Pus was present in the left middle ear. The third case closely resembled the other two.

LANGMANN, New York.

TWO CASES OF CONGENITAL OEDEMA. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **25:** 956 (May) 1932.

The first case reported was in an infant 5 months old who showed severe anemia. The hair was coarse and sparse, and there were redundant folds of skin on the posterior aspect of the neck and edema of the vulva and dorsa of the feet. The spleen was enlarged, the Wassermann test was negative and the urine was normal.

The second case, also in a baby of 5 months, showed simply edema limited to the feet in an otherwise normal infant.

WILLIAMSON, New Orleans.

PNEUMOCOCCIC MENINGITIS IN THE NEW-BORN. G. SCHREIBER and R. KOHN, Arch. de méd. d. enf. **35:**352 (June) 1932.

Occasional cases of meningitis in the new-born have been reported, but the infection is nevertheless extremely rare. Lequeux has reported a streptococcic invasion of the fulminating type in an infant of 12 days; Herrman has described a further case and has found reports of eleven others in babies less than 15 days of age scattered through the literature. Most of these were identified post mortem, and the bacteria involved included Bacillus coli, B. lactis-aerogenes, B. pyocyaneus and B. mucosus-capsulatus. In Herrman's patient the pneumococcus was the infecting agent.

The authors report a case in an infant with negative birth history seized on the second day of life with respiratory embarrassment, followed by convulsions, hyperpyrexia and diarrhea. The spinal fluid was cloudy, but pressure was not increased, and examination revealed the pneumococcus with innumerable pus cells. Death occurred on the ninth day. The writers believe that antenatal infection can be excluded, and present the hypothesis of contamination by carrier, probably through the baby's father, who had sustained an attack of pleuropneumonia some months before.

AMESSE, Denver.

DEATH FROM MENINGEAL HEMORRHAGE IN INFANTS DELIVERED BY CESAREAN SECTION. VORON, BANSSILLON and PIGEAUD, Bull. Soc. d'obst. et de gynéc. **21:**39 (Feb.) 1932.

The authors reported two cases. In the first, a trial labor was attempted in a woman with a flattened and generally contracted pelvis who had previously been delivered of two dead infants by means of forceps. After fourteen hours, the membranes were ruptured, but the head remained high. At this time, the infants's heart tones were normal, and a low cesarean section was performed. When the uterus was opened, meconium escaped and a pale, dead child weighing 3,200 Gm. was extracted. Necropsy disclosed only a diffuse meningeal hemorrhage, more marked below the tentorium.

In the second case the mother had previously delivered six infants. Three died following forceps extraction. The fourth infant was delivered by breech extraction, it lived six months and died in convulsions. In the fourth and fifth pregnancies labor was induced at eight and one-half months. The fifth infant was born dead, and a sixth infant lived only a few hours. The mother had a flattened and generally contracted pelvis. The Wassermann reaction of the blood was negative, but she had received treatments irregularly because of sus-

pected congenital syphilis. In the seventh pregnancy she went into labor fifteen days before term, and after twenty hours the membranes were unruptured. The infant's heart tones were normal. A low cesarean section was performed; the amniotic fluid was clear, and a pale, dead infant weighing 2,930 Gm. was delivered. At necropsy there was a hemorrhagic subdural infiltration without a real subdural layer of blood clot. Microscopically, there was a perivascular extravasation of blood without actual rupture of the vessels. In some sections there were areas of perivascular infiltration the exact nature of which could not be determined.

It was the authors' impression that these two deaths were due to hemorrhage secondary to intra-uterine infection of the fetus, probably syphilis in the second case.

ABSTRACTOR'S COMMENT.—In view of the type of obstetrics practiced in these two cases, it seems probable that the infants died of asphyxia following too prolonged labor and that the hemorrhages resulted from this rather than from problematic infection.

GLASER, Rochester, N. Y.

CONGENITAL GOITER IN A NEW-BORN INFANT OF A MOTHER WITH GOITER. VORON and BROCHIER, Bull. Soc. d'obst. et de gynéc. **21**:128 (Feb.) 1932.

The mother, 21 years of age, had a goiter of six years' duration without any symptoms of toxicity. The infant was delivered normally and weighed 3,170 Gm. The infant's goiter was about the size of a pigeon's egg, most of the enlargement being in the left lobe. Apparently, such cases are not rare in France. In the discussion of this case, Dr. Plauchu stated that he had observed a case in which the infant died because of pressure of the goiter.

GLASER, Rochester, N. Y.

REPORT OF A CASE OF FIBRO-ANGIOMA IN A NEW-BORN INFANT. OTTAVIO LARINI, Clin. pediat. **13**:671 (Aug.) 1931.

The author describes a case of fibro-angioma adjacent to the right breast in a new-born boy. The mass was well defined at birth and showed a definite subcutaneous point of origin. The histologic structure is described, and two illustrative photomicrographs are given, which show in particular that the subcutaneous fatty tissue participated in no way in the formation of the tumor.

SIGNORELLI, New Orleans.

DISTURBANCES OF NUTRITION DUE TO ACUTE INFECTION IN NEW-BORN INFANTS. A. HOTZ, Jahrb. f. Kinderh. **135**:129 (April) 1932.

The author describes two epidemics ("endemics") of acute nutritional disturbance, which he believes were due to infection with Staphylococcus aureus. One epidemic was traced to a granulating furuncle on the neck of a nurse; the other, to an infected mother. Of the newly born infants, four died of intestinal sepsis; projectile vomiting was observed, and at autopsy the pylorus was normal. Of the seven young infants, none died. Repeated intramuscular injection of whole blood seemed definitely of value.

CLAUSEN, Rochester, N. Y.

THE ATTITUDE AND THE FORM OF THE HEAD OF THE FETUS IN BREECH PRESENTATION IN UTERO. E. KEHRER, Ztschr. f. Geburtsh. u. Gynäk. **101**:32 (March 24) 1932.

The famous frozen section of Waldeyer (1886) showed the fetus in "double breech presentation," the chin flexed to the chest and the head as round as a ball. Since that time this flexed attitude and round head were considered the normal and average findings in breech presentation. The röentgenogrgams of Warnekros (1919) proved, however, that the fetus in utero is not in such a constrained atti-

tude, but in an easy position, with little or no flexion except the limbs, which are slightly flexed. Fenty published a drawing in 1767 which showed the child in single breech presentation.

The author made investigations on three preparations of pregnant uteri and on one hundred and eleven pregnant women, the fetus being in breech presentation. In fifty of the cases a roentgenologic examination was done. All three preparations showed the child in single breech presentation.

The author found that the form of the head in breech presentations often is dolichocephalic. This observation has been made by former investigators also, contrasting the general opinion that the head in breech presentations is round.

The author found a dolichocephalic head in fifty-one of seventy-five cases of primiparae and in twenty-five of thirty-three cases of multiparae.

In addition to the dolichocephalic condition, one often finds an oblateness of one side of the skull and, therefore, an asymmetry of the head. Furthermore, a flexion of the head to one side can be observed in many cases.

The caput obstipum musculare is much more frequent in children born in breech presentation than in those born in head presentation, due to the intrauterine pressure of the fundus uteri on the head.

Deflexion-attitude is another condition that may frequently be found in breech presentation. In 25 per cent of his cases the author found the attitude similar to that found in median vertex presentation; in 45 per cent, an attitude similar to that found in forehead presentation; in 10 per cent, an attitude similar to that found in brow presentation and in 5 per cent, an attitude similar to that found in face presentation. Real flexion was found in not more than 15 per cent. In some cases this flexion-attitude was marked.

The single breech presentation was found in 86.1 per cent of the patients examined roentgenologically during pregnancy, and in 78.6 per cent during labor, so it apparently is more frequent during pregnancy. It is certainly much more common than it is thought to be. The author proves that this attitude is more physiologic and convenient for the fetus in utero than the double breech presentation, which has been considered the normal presentation up to the present time.

ADAIR and SIEDENTOPF, Chicago.

Acute Infections

QUININE ANALYSIS OF THE BLOOD WITH REFERENCE TO TREATMENT OF MALARIA. J. H. ST. JOHN, Am. J. Trop. Med. **12**:101 (March) 1932.

St. John carried out experiments in which 30 grains (1.9 Gm.) of quinine was administered orally to patients in various amounts over varying periods of time. He then determined the time for the maximum concentration of quinine to take place in the blood stream. He found that it varied with different persons, and that the maximum concentration of quinine was dependent on the total amount of quinine given, irrespective of the spacing of the doses. If 30 grains was given in one dose, the concentration of quinine in the blood serum reached a maximum in a few hours, in the majority of cases, and then decreased. If the quinine was given in smaller doses, the maximum concentration was reached much later. After the maximum concentration was once obtained, it could, in the majority of instances, be maintained indefinitely by proper doses properly spaced. He also found that in a few patients there was not developed or maintained a blood concentration of quinine as high as in others, while in some there was developed and maintained a maximum concentration in excess of the average.

BURPEE, Augusta, Ga.

STAPHYLOCOCCUS ALBUS SEPTICEMIA. HAROLD R. ROEHM, Arch. Pediat. **49**:165 (March) 1932.

Attention is called to the scarcity of literature on Staphylococcus albus septicemia. A case of Staphylococcus albus septicemia is presented in which there was recovery without complications. Treatment consisted of transfusions of blood from three different donors. A second case of Staphylococcus albus septicemia occurring in a 4 weeks old infant is also reported, this case resulting in death.

WADDELL, JR., University, Va.

AN UNUSUAL CASE OF EPIDEMIC MUMPS COMPLICATED BY GANGRENOUS APPENDICITIS. ARTHUR S. SANDLER and BURTON A. FINNE, Arch. Pediat. **49**:175 (March) 1932.

A case of epidemic mumps complicated by acute gangrenous appendicitis is reported. Attention is called to similar reports in the literature.

WADDELL, JR., University, Va.

POLIOMYELITIS: I. PRODUCTION OF ANTIVIRAL SERUMS BY INOCULATION OF GOATS AND SHEEP WITH THE VIRUS OF POLIOMYELITIS. BEATRICE F. HOWITT, J. Infect. Dis. **50**:26 (Jan.) 1932.

The author's conclusion was: "The prolonged immunization of two goats and a sheep with poliomyelitic virus over a period of years resulted in the development of antiviral substances that were capable of protecting monkeys against infection, both when tested by the different methods of in vitro neutralization and when used therapeutically or as a prophylactic, in a certain number of instances."

TOOMEY, Cleveland.

OCCURRENCE OF DIPHTHEROIDS IN BLOOD CULTURES. LUTHER THOMPSON, J. Infect. Dis. **50**:69 (Jan.) 1932.

Of 1,079 blood cultures, 33, or 3 per cent, gave a growth of diphtheroids. These organisms were not mutated forms of streptococci, since they did not revert to that form after subculturing in broth. Their appearance in cultures can be ignored as they are not pathogenic.

TOOMEY, Cleveland.

MEASLES IMMUNIZATION WITH PARENT SERUM IN PRIVATE PRACTICE. WILLIAM WILLIS ANDERSON, J. South Carolina M. A. **28**:31 (Feb.) 1932.

Dr. Anderson reports five cases of measles between December, 1930, and March, 1931, in children under his observation who had been exposed to measles. Parent's serum was used in forty-one cases. The Wassermann reaction was obtained in most cases, but the result of this test was not awaited in all cases before the serum was used.

Twenty-four children, or 58.4 per cent, received complete protection. Modified or attenuated measles occurred in 29.2 per cent. One child had bilateral otitis media. Of the sixteen patients not treated, otitis media developed in three and bronchopneumonia in seven.

The reaction to parent's serum was neglible, except in one case. A history of measles in the father or mother was always elicited.

The author concludes: 1. Parent's serum will prevent measles in a large percentage of children when given early enough and in large enough amounts. 2. In children who are in good physical condition it is necessary to give only enough serum (about 0.25 cc. per pound of body weight) to allow them to have attenuated measles, in this way insuring a permanent immunity.

WESTON, JR., Columbia, S. C.

GONORRHEAL VULVO-VAGINITIS AND OPHTHALMITIS IN CHILDREN: REPORT OF THREE CASES. WILLIAM WESTON, J. South Carolina M. A. **28**:56 (March) 1932.

Emphasis is laid on the isolation of all girls in whom cases occur until a vaginal smear has been made to determine the presence or absence of gonococci.

WESTON, JR., Columbia, S. C.

ACUTE POLIOMYELITIS. HOWARD J. HARTMAN, M. J. & Rec. **135**:26 (Jan. 6) 1932.

In this article the author states that the preparalytic stage of poliomyelitis presents a distinct clinical entity; that diagnosis can and should be made early, before the ensuing paralysis makes it clear to all; that human convalescent serum administered intraspinally or intramuscularly is of definite value in preventing paralytic sequelae; that if convalescent serum is not available, Rosenow's serum should be used, and that the intramuscular route of administration of either serum is simple, safe and sufficiently efficacious to justify its use during an epidemic.

WILLIAMSON, New Orleans.

THE STANDARDIZATION OF SCARLET FEVER STREPTOCOCCUS ANTITOXIN. M. V. VELDEE, Pub. Health Rep. **47**:1043 (May 6) 1932.

The author has developed a practical laboratory animal method of measuring the potency of scarlet fever streptococcus toxins and antitoxins. He uses the white rabbit and makes the injections in the ear. Readings are made in twenty-four and forty-eight hours. The end-results are more definite than those obtained on human subjects. The effect of the neutralizing value of different antitoxins showed that the multistrained antitoxins neutralized in the same manner as the single strain.

SANFORD, Chicago.

A STUDY OF THE SLEEPING-PULSE-RATE IN RHEUMATIC CHILDREN. BERNARD SCHLESINGER, Quart. J. Med. **1**:49 (Jan.) 1932.

Schlesinger points out that normally the pulse rate during sleep is on an average 10 beats per minute slower than that when the subject is alert or awake. A rapid alert pulse rate not accompanied by an increase during sleep points to nervous tachycardia. In active carditis in the absence of fever, the pulse rate during sleep approximates that during waking hours. The author points out that the pulse count must be taken without partially awakening the patient.

BRADFORD, Rochester, N. Y.

EPIDEMIC ACUTE RHEUMATISM IN A PUBLIC SCHOOL. W. H. BRADLEY, Quart. J. Med. **1**:79 (Jan.) 1932.

Two distinct outbreaks of rheumatism occurred in 25 boys in a school of 340 between May, 1929, and April, 1931. Prior to that date no case of rheumatism had been recognized in this school during a period of forty years. Each outbreak of rheumatism followed an epidemic of hemolytic streptococcal sore throat, but the causal streptococci were of two distinct strains. It is suggested by the author that rheumatism occurred in those who had been incompletely immunized by a first contact with streptococci and in whom allergy to that organism had developed.

BRADFORD, Rochester, N. Y.

HERPES ZOSTER AND VARICELLA. CONVALESCENT SEROTHERAPY. L. CORNIL and F. BLANC, Rev. neurol. **2**:123 (July) 1931.

The patient's illness began on December 12 with right facial neuralgia, which was followed on December 14 by a mild chickenpox eruption. Five days after

the onset of pain, herpetic vesicles appeared in the first and second divisions; on December 20, there was severe generalized varicella; on December 31, there was complete ophthalmoplegia. A recurrence of facial neuralgia, with neuroparalytic keratitis occurred on January 12; there was a mild recurrence of varicella in March. On December 22, while the varicella was at its height, 20 cc. of blood from a patient convalescing from herpes zoster was injected subcutaneously, with complete relief of pain and a marked turn for the better. The close relationship between herpes zoster and varicella is again emphasized by this case.

FREEMAN, Washington, D. C. [ARCH. NEUROL. & Psychiat.]

A CASE OF PURPURA FULMINANS IN THE CONVALESCENCE OF SCARLET FEVER. EUGENIA YANNUZZI, Arch. de pediat. d. Uruguay **2**:27 (Jan.) 1932.

This condition occurred in a girl 12 years of age, who had had a moderately severe attack of scarlet fever. There was considerable adenopathy, with a rather large swelling at the angle of the jaw. During convalescence the most intense fulminating purpura developed, with marked hemoptysis, bleeding from the nose and mouth and profuse hemorrhagic eruption covering the entire body. Deep coma with tonic convulsions developed.

The case terminated fatally. The entire attack lasted about forty hours. No form of treatment seemed to stay the fatal progress of the disorder.

SCHLUTZ, Chicago.

ANTIDIPHTHERITIC VACCINATION IN BUENOS AIRES. PAUL CIBILS AGUIRRE, Bol. Inst. internac. am. de protec. a la infancia **5**:321 (Jan.) 1932.

Substantiating the efficiency of antidiphtheritic vaccination, Aguirre states that neither the Rocca Preventorium, with 500 inmates, nor the Necochea Seaside Colony, with 3,200 children, reported any case of diphtheria after vaccination. At the Colony, 140 children were vaccinated and 25 were not in 1928; 5 of the latter contracted diphtheria. Of 2,000 children of the Patronato de la Infancia, more than 80 contracted diphtheria, but none of the cases occurred among children properly vaccinated. The results of 95 per cent of the Schick tests given after vaccination at the Patronato de la Infancia were negative. It is not illogical to state that the immunity conferred by the anatoxin persists for many years and very likely through life. During the campaign of the Board of Public Health, 60,000 inoculations were administered to 16,000 children. The author recommends the subcutaneous procedure as the most advantageous.

Four cases of diphtheria among vaccinated children were reported, but some of these children were incompletely vaccinated; this is not a surprising fact, since the method employed leaves from 2 to 5 per cent of children not immunized.

The author recommends adherence to the same technic: first, subcutaneous injection of 0.5 cc. of anatoxin; second, injection of 1 cc. after three weeks; third, injection of 1.5 cc. after two more weeks. When a stronger anatoxin is obtained, the ideal will be to diminish the number of injections.

It would be better not to make vaccination compulsory at present; it is preferable to wait until the public at large and all the physicians are persuaded of its efficiency.

EDITOR'S SUMMARY.

THE SEASONS AND INFECTIOUS DISEASES. MORITZ DEMANT, Kinderärztl. Praxis **2**:221 (May) 1931.

The morbidity and mortality curves for pneumonia show the highest peaks in March, April and May. Similar curves for measles parallel those of pneumonia. In pertussis, the curves follow the same general outline of those for pneumonia, but not nearly so closely as do those for measles. Because these three infections are predominantly diseases of the respiratory tract, their curves would rather be expected to coincide. The curves for diphtheria show a summer valley similar to

the other three diseases, but the peaks appear in November, December and January. In pneumonia, measles, pertussis and diphtheria, the morbidity and mortality curves roughly parallel each other, but it is otherwise with scarlet fever. In this disease, the mortality tables show a summer valley which is decidedly flattened; in fact, the whole curve is more of the plateau type. The morbidity curve for scarlet fever, on the other hand, shows a peak in October, November and December over 50 per cent higher than in any other three month period. The author discusses the various factors influencing these curves, but declines to give any definite conclusions.

HUENEKENS, Minneapolis.

DIFFERENT DIPHTHERIA TOXOID PREPARATIONS: THEIR VALUE IN EXPERIMENTS ON ANIMALS. W. KOLLE, R. PRIGGE and W. FISCHER, Med. Klin. **28**:41 (Jan. 8) 1932.

Rather extensive experiments have been used for determining the value of formaldehyde diphtheria toxoid preparations. All preparations were made from the same toxin and by the same method. Different preparations have shown differences in the effectiveness of immunization. The authors therefore think that toxoid preparations should be tested not only for toxicity but also for effectiveness. A standard preparation can be used as a measure in comparison. Within certain limits small doses of toxoid preparations give a lesser degree of immunity than high doses. Immunity following repeated injections lasted longer than immunity after one injection. That is to say, two injections produced a longer period of immunity than one injection, and three injections a longer period of immunity than two. If three equal doses of toxoid were injected into animals, the animals became more immune to the double lethal dose than if the same dose were given in only one or two injections.

ZENTAY, St. Louis.

THE VACCINE TREATMENT OF WHOOPING COUGH. M. WEICHSEL, Monatschr. f. Kinderh. **52**:106 (Feb.) 1932.

In a study of fifty patients treated with the Bordet vaccine, the writer could not demonstrate any appreciable benefit.

GERSTLEY, Chicago.

THE VACCINE TREATMENT OF WHOOPING COUGH. E. G. WESTENDORFF and H. GENTZSCH, Monatschr. f. Kinderh. **52**:261, 1932.

In this study, the first section is written by Westendorff. He reviews the literature on whooping cough and then reports a study of thirty-five cases. Fifteen of these were treated by injections of foreign protein and the remaining twenty by injections of the specific vaccine. He can see no effect of either treatment on the course of the disease.

Gentzsch, on the other hand, reports forty-five cases in which the specific whooping cough vaccine was given. He believes that in twenty-six of these there was a definite shortening of the disease proportionate to the promptness with which the vaccine was given. He believes that the treatment is of value as a prophylactic, but he has seen no good results in nurslings. He also believes the inoculations help the appetite and nutrition.

GERSTLEY, Chicago.

EFFECT OF INTERCURRENT INFECTIONS ON TETANUS. A. HOCHWALD and O. SAXL, Ztschr. f. Kinderh. **52**:260, 1932.

In four cases of tetanus the symptoms were markedly diminished by intercurrent infections (measles, pneumonia). Three other cases are cited from the literature. The mechanism of this effect is thought to be that of "toxin antagonism."

SHELLING, Baltimore.

THE PROBLEM OF TOXIC DIPHTHERIA: II. VIRULENCE OF DIPHTHERIA BACILLI FROM VARIOUS SOURCES. G. HEISSEN, Ztschr. f. Kinderh. **52:** 372, 1932.

Virulent and nonvirulent strains of diphtheria bacilli were passed through nutrient mediums. The passage of malignant strains more than one hundred times through Braun's medium did not affect the virulence. When inoculated into animals, the toxic strains produced toxic and lethal results much sooner than the avirulent strains isolated from the oronasopharynx of apparently normal persons. The latter strains, however, produced stronger local reactions. Antitoxin neutralized both strains to about the same degree. The importance of early administration of antitoxin is stressed.

SHELLING, Baltimore.

THE PROBLEM OF TOXIC DIPHTHERIA: III. THE CONSTITUTIONAL EFFECT ON THE CHARACTER OF DIPHTHERIA BACILLI. FRIEDRICH GRÜNEBERG, Ztschr. f. Kinderh. **52:**423, 1932.

It is claimed by Koschta that the toxicity of avirulent strains of diphtheria bacilli may be increased by passage through a medium containing human serum, especially serum from a patient with toxic diphtheria. Grüneberg isolated diphtheria bacilli from six cases of mild diphtheria and grew them on mediums containing mutton or normal human serum and also serum from patients with mild and patients with malignant diphtheria. Morphologically, no difference was found in the organisms grown on the different mediums. The toxicity of the organisms varied with the source rather than with the character of the medium. The toxicity of the avirulent types was not increased by passage through serum of patients with toxic diphtheria. The results and conclusions of Koschta could not be corroborated.

SHELLING, Baltimore.

THE EFFECTIVENESS OF DIPHTHERIA IMMUNIZATION IN A TOWN IN HUNGARY. P. ORMOS and I. FÜLÖP, Orvosi hetil. **75:**861, 1931.

In a medium-sized town in Hungary, immunization against diphtheria was introduced. Of 10,000 children between the ages of 1 and 15, 2,260 were immunized in the first period. Ramon's anatoxin was used for immunization. Of the 2,260 children immunized, diphtheria developed in 1 within the next six months. During the same period among the 7,740 who were not immunized, 42 cases of diphtheria were found. In the next series, 5,587 children were immunized, and of these, diphtheria developed in 4, while during the same period among the 4,413 nonimmunized children, 17 contracted diphtheritic infection. The cases among the immunized children were very mild, and no deaths occurred. The nonimmunized children had more severe forms of diphtheria, and 2 deaths occurred. Comparison of the frequency in the two groups shows that among the nonimmunized children in the first series, diphtheria occurred twelve times more often than among the immunized. In the second series it occurred five and one-half times more frequently. Taking the total number of children, the morbidity among the immunized was 0.6 per thousand; among the nonimmunized, 5.8 per thousand. These figures show clearly the value of immunization against diphtheria.

ZENTAY, St. Louis.

MYODEGENERATION OF THE HEART FOLLOWING DIPHTHERITIC VULVOVAGINITIS. P. KISS, Orvosi hetil. **75:**903, 1931.

Diphtheritic vulvitis and vulvovaginitis may occur in primary or secondary form. The prognosis of these conditions is in no way more favorable than that of diphtheritic infections in the throat. Muscular degeneration of the heart may develop in connection with diphtheritic vulvovaginitis in the same manner as in

any other localization of the infection. Serum treatment in diphtheritic vulvovaginitis should be governed by the same principles as it is in other forms of diphtheritic infections.

ZENTAY, St. Louis.

OCCURRENCE OF OTITIS MEDIA FOLLOWING SCARLET FEVER. T. LAIB, Orvosi hetil. **75**:995, 1931.

The author studied statistically the occurrence of oral complications in the different epidemics of scarlet fever observed in a contagious hospital in Budapest since 1914. The frequency of otitis media following scarlet fever seems to be very variable in the different epidemics. It seems to depend mostly on the severity of the epidemic, on the so-called genus epidemicus. Early paracentesis is indicated, as mastoiditis is more frequent when spontaneous perforation of the membrane takes place. Otitis media usually appears in the second or third week, often on one side first and on the other side somewhat later.

ZENTAY, St. Louis.

SEVERE CASE OF SCARLET FEVER. H. KODYSZ, Pediat. polska **11**:182 (May-June) 1931.

The author reports a severe case of scarlet fever with complications in an 11 year old girl. She recovered after treatment with antitoxin, neoarsphenamine and vaccine.

KRUPINSKI, Chicago.

THE CHARACTER OF DIPHTHERIA EPIDEMICS IN WARSAW. J. BOGDANOWICZ and T. WELFLE, Pediat. polska **11**:231 (July-Aug.) 1931.

The authors review the epidemics of diphtheria occurring from 1880 to 1930, showing that there was a decrease in the number of occurrences and of deaths. There was a slight increase every ten years and then a decrease until 1925. From 1925 to 1930 Warsaw experienced a severe epidemic. The authors give a thorough review of diphtheria, with a discussion of epidemiology, morbidity and mortality. Jewish children have a less toxic type of diphtheria. In the treatment, besides diphtheria antitoxin, in some cases antimeningococcus serum and arsenical preparations, like neoarsphenamine and sugar and insulin are used, with good results.

KRUPINSKI, Chicago.

GONORRHEA AMONG YOUNG GIRLS. K. A. KARISHEV, Pediatriya **14**:331, 1930.

The author had under observation ninety young girls afflicted with gonorrhea. Among these patients, from 24 to 27 per cent were children of workmen; from 30 to 33 per cent, of clericals; from 12 to 13 per cent, of doctors; from 4 to 4.5 per cent, of college students; from 4 to 4.5 per cent, of artisans; from 2 to 2.5 per cent, of unemployed; from 4 to 4.5 per cent, of merchants. From 10 to 11 per cent were waifs.

From 20 to 22 per cent were below 5 years of age; from 50 to 56 per cent, from 5 to 10 years, and the remainder, above 10 years.

Of the seventy-five girls not infected through sexual contact, 50 per cent acquired the disease from their mothers; 11 per cent, from their sisters; 15 per cent, from housemaids, and 12 per cent, from friends. This is largely due to congested dwelling accommodations and use of toilet articles in common.

Fifteen of the girls acquired the disease as a result of sexual intercourse. Ten of these were waifs who were professional prostitutes; the others lived in homes. One of these girls, 15 years old, lived with an adult; two lived with their school boy friends. One related that she was dragged into her girl friend's home and attacked by boys as a punishment for her exaggerated modesty.

The study clearly indicates the necessity for more wholesome sex education among children, for hygiene of sick mothers beginning with the period of expectancy, and for relief from congestion in dwellings.

YAMPOLSKY, Atlanta, Ga.

CASE OF CHICKENPOX WITH SUBCUTANEOUS HEMORRHAGES. N. TAKAMATSU, J. Pediat. (Tokyo), Feb. 20, 1932, no. 381, p. 265.

The author reports the case of an 11 months' old infant, in whom purpuric spots and large areas of subcutaneous hemorrhages developed during convalescence from chickenpox. The hemorrhagic spots gradually increased in size, until the largest area occupied nearly the entire flexor surface of the left arm. Suggillations were also seen to develop on both cheeks. The trunk and the scalp were free from the purpuric spots. The extremities were edematous. The examination of the blood showed slight anemia (72 per cent Sahli), with polyglobulism (red blood cells, 6,790,000). The bleeding time was 3.5 minutes, while the coagulation time was 17.5 minutes. Platelets were 149,000, and the tourniquet test was negative. Thus the condition was not due to disease of the capillaries, but rather to that of the blood itself in some unknown way. The author used an anticoagulent to advantage.

KATO, Chicago.

Chronic Infections

THE EARLY CELLULAR REACTIONS IN THE LUNGS OF RABBITS INJECTED INTRAVENOUSLY WITH HUMAN TUBERCLE BACILLI. ARTHUR J. VORWARD, Am. Rev. Tuberc. **25**:74 (Jan.) 1932.

The cells in rabbits that respond first to an intravenous injection of tubercle bacilli of human type (0.1 mg. per kilogram of animal weight) are the polymorphonuclear leukocytes. This reaction, while transitory, is not one of negligible significance, for it is through the agency of these cells that the site of subsequent development of the tubercle is determined. These cells phagocytose the tubercle bacilli in the blood stream, and stagnate in small accumulations in the capillaries where the current is slow. In this way injected bacilli are concentrated and localized. The localized accumulations of polymorphonuclear leukocytes form the groundwork from which the epithelioid tubercles develop. Mononuclear exudate cells are preponderant in the cellular response after the first few hours (from fourteen to eighteen hours on). They mingle with the polymorphonuclear leukocytes, phagocytose and digest them and take up their content of tubercle bacilli. In this way, by replacement of the leukocytic mass, the mononuclear cell tubercle, ultimately the epithelioid tubercle, develops. The increase in mononuclear exudate cells in the field of inflammation, in the almost total absence of mitotic figures in such foci, indicates that the majority of reacting cells of this type are hematogenous in origin.

SMITH, Ogden, Utah.

TUBERCULOSIS IN CHILDREN. H. D. CHADWICK, J. Michigan M. Soc. **30**:15 (Jan.) 1931.

In this paper the childhood and adult types of pulmonary tuberculosis are differentiated as follows:

The childhood type is rare in adults; it is the result of a primary infection, may be in any part of the lung, always involves the associated lymph nodes, tends after caseation to calcification or fibrosis, resolves after infiltration and is of good prognosis. The adult type may be found in children; it is a reinfection not usually involving associated nodes, is apical, tends to cavitation and fibrosis and has a poor prognosis in childhood. The infiltrated areas tend to resolve with some fibrosis.

In the history in children the author regards contact as of great importance, and points out that no symptoms may have been present. He mentions the fact that

tuberculous pleurisies with effusion are not uncommon symptoms of beginning disease in children. A roentgenogram is considered indispensable in diagnosis; it will show either parenchymal or glandular changes, or both. The author feels that children with tuberculosis should be strictly isolated from contact with other children who have the disease, but that tuberculous children with tuberculosis, but without open lesions, need not be kept from school.

SMITH, Ann Arbor, Mich.

OPERATIVE TREATMENT OF JOINT TUBERCULOSIS. MELVIN S. HENDERSON, Minnesota Med. **15**:141 (March) 1932.

Operative treatment has its greatest field of influence among adults; conservative treatment is best suited to children. The child's time is not so valuable as that of the adult; he has no responsibilities and often, in healthy and happy surroundings, overcomes the disease. Institutions are readily available for the child, in which he may stay indefinitely, whereas this is not true for the adult.

HUENEKENS, Minneapolis.

MANTOUX OBSERVATIONS IN FIVE HUNDRED AND TWENTY INDIAN CHILDREN. HOMER DAVIS, Nebraska M. J. **17**:98 (March) 1932.

Indian children were tested for tuberculosis by means of the Mantoux reaction; 0.1 cc. of 1:1,000 old tuberculin was used. Of the 520 examined, 71.9 per cent gave positive reactions. Equal percentages of boys and girls had positive reactions. Twenty-eight were classed as reactors of grade IV (a reaction of more than 4 cm.). These with three others who had strong reactions of grade III were studied in detail with x-rays and by daily observation. Of this class, 27 were girls, and only 4, boys. The age varied from 9 to 20 years. Only 8 presented an appearance of undernourishment. There was a history of direct exposure in all cases of this group. The author concludes that tuberculosis in Indian children of school age is much more prevalent than is apparent on observation.

HAMILTON, Omaha.

THE SPECIFICITY OF SKIN REACTIONS IN MAN IN RELATION TO TUBERCULOUS INFECTION. B. P. D'ARCY HART, Quart. J. Med. **1**:49 (Jan.) 1932.

The author reviews the literature concerning the association of tuberculin sensitivity in man with cutaneous reactivity to substances not derived from the tubercle bacillus.

He presents the results of a comparison of various samples of glycerinated veal peptone broth with old tuberculin as reactive substances in the skins of tuberculous and of nontuberculous subjects.

The incidence of skin sensitivity to meat extract in the form of glycerinated veal broth was found to be practically identical with the incidence of hypersensitiveness to tuberculin. Nearly every person sensitive to old tuberculin (1:1,000) reacted to glycerinated veal broth when a very active sample and an adequate dose were used. The intensity of the reactions in persons sensitive to broth was found in the main to run parallel with the intensity of the tuberculin reactions. The property of eliciting the tuberculin-like skin reactions was found to be present in the peptone fraction of broth and in the veal extract fraction of glycerinated veal broth.

BRADFORD, Rochester, N. Y.

TUBERCULOUS PLEURISY IN INFANCY. A. MAZZEO, Pediatria **60**:26 (Jan. 1) 1932.

In this paper are reported two cases of serous pleurisy of tuberculous nature in infants from 4 to 9 months of age, respectively. The distinct differences between

these two cases as regards clinical course and final outcome, permitting certain considerations regarding pathogenesis, are: In the first case, a large tuberculous lesion in the posterior margin of the left lung led to the possibility of an infection of the pleural cavity by contiguity; in the second case, the clinical symptoms and the contemporary manifestations of bony and cutaneous lesions led to the hypothesis that there was here an allergic infection of the pleura dependent on the general tuberculous infection of the patient, since there was a complete absence of pulmonary lesions. Not only could pulmonary lesions not be demonstrated clinically, but the rapid and uneventful complete clinical cure points to the improbability of pulmonary lesions.

SIGNORELLI, New Orleans.

TUBERCULOSIS IN CHILDHOOD. LUIS MORQUIO, Bol. Soc. cubana de pediat. **4**:25 (Jan.) 1932.

In a public address, this eminent South American clinician states the following conclusions: Contact infection is the chief cause of tuberculosis in childhood; the disease assumes grave aspects, with reference to both its location and the child's resistance to it, depending on the age of the child, the environmental conditions and the individual constitutional characteristics of the child. He believes that uniform practice of the cutaneous tuberculin test is the best means of detecting latent forms. In this way, attention is attracted to the affected person, and an opportunity is given to place him under favorable conditions of environment and treatment. The treatment of tuberculosis in childhood from the standpoint of the physician is, above all, prophylactic and hygienic.

F. W. SCHLUTZ, Chicago.

THE THERAPEUTICS AND PROPHYLAXIS OF THE CHILDREN OF LEPERS. ORESTE PENTAGNA, Medicamenta **6**:38 (July) 1931.

The author reviews the various forms of treatment for leprosy and outlines the work done by the "Pro-Infantia" institute in São Paulo with regard to the treatment of children of lepers. He gives a clinical record of five families of lepers in which some of the children showed B. hansenii, and of their resultant cure at the institute.

SANFORD, Chicago.

RETROGRESSION OF SEDIMENTATION REACTION AND PROGRESSIVE TUBERCULOSIS. O. GSELL, Deutsches Arch. f. klin. Med. **172**:443 (March 21) 1932.

In the course of experimental tuberculosis of guinea-pigs, the sedimentation reaction showed, after an initial marked increase, a return to the normal rate and, despite an advancing tuberculous process, continued without acceleration even up to the time of death from tuberculosis. The percentage of globulin, as determined by a refractoviscosimetric method, showed a marked increase at the same time but, even in advancing disease, remained elevated. Only a part of the animals showed a diminution in the percentage of globulin even in the terminal stages. Fibrinogen, after an initial rise, decreased with the sedimentation reaction, the decrease continuing up to the death of the animals. Tuberculous guinea-pigs in which the sedimentation reaction has returned to normal do not show an elevation after inoculation with a trichophyton as do normal guinea-pigs.

In the last months of severe, chronic pulmonary tuberculosis, when resistance has disappeared, there is a decrease of the sedimentation reaction. The percentage of globulin remains high despite the decrease of the absolute globulin content with the decrease in total serum protein. This discrepancy between the sedimentation reaction and the percentage of globulin is an unfavorable prognostic sign. In miliary tuberculosis, the sedimentation reaction returns to normal in about one fourth of all cases. The regression is less frequently seen in tuberculous meningitis because of the earlier death of the patient.

DOOLEY, Kent, Conn.

THE INFLUENCE OF INTERCURRENT INFECTIONS ON TUBERCULOSIS OF THE CHILD. HELMUT LIESEGANG, Gesundhfürs. f. d. Kindesalt. **7**:33 (Feb.) 1932.

The opinion of Noeggerath and Eckstein that there is no consistent activation of tuberculosis by measles is substantiated. In individual cases this may occur, but it is by no means a common result.

REICHLE, Cleveland.

CHRONIC APPENDICITIS AND CONGENITAL SYPHILIS IN THE CHILD. V. MIKULOWSKI, Jahrb. f. Kinderh. **134**:345 (Feb.) 1932.

Four cases of appendicitis in which congenital syphilis was found are reported; antisyphilitic treatment resulted in relief from symptoms. Detailed discussion as to the possibility in these cases of a syphilitic involvement of the vegetative nervous system is given.

CLAUSEN, Rochester, N. Y.

THE LOCAL BLOOD PICTURE IN CHILDREN'S TUBERCULOSIS. GERTRUD KEHLING, Monatschr. f. Kinderh. **52**:239, 1932.

Kehling made blood counts from drops of blood obtained in the locality of a positive Pirquet reaction. She concludes that in this local blood picture there is always an increase in the white cells. The relation of the white cells to each other is the same as in the general blood picture. She does not agree with Helmreich that changes in the blood picture are typical of any stage of tuberculosis. Absolute or relative lymphocytosis may occur in any stage of tuberculosis. Absence of this finding in her series occurred only in those cases in which the prognosis was bad. She concludes that this local blood picture is of no value in diagnosis, but may have some slight value as a prognostic sign.

GERSTLEY, Chicago.

CONGENITAL TUBERCULOSIS. J. SCHOEDEL, München. med. Wchnschr. **78**:705 (April 24) 1931.

A woman, aged 22, with miliary pulmonary tuberculosis gave birth to an apparently healthy infant weighing 2,650 Gm. Chloroform anesthesia was used during the delivery. The infant was removed from the delivery room twenty minutes after birth and had no further contact with the mother. The mother died a few days post partum. At 4 months of age the infant had slight elevations of temperature, but the Moro tuberculin test was negative. During the following month the infant coughed occasionally and became pale. At 5 months of age the Moro reaction was positive and a roentgenogram showed a moderate number of small shadows in both lungs.

BRAHDY, Mount Vernon, N. Y.

A CASE OF CONGENITAL MYXEDEMA AND CONGENITAL SYPHILIS WITH SUCCESSFUL TREATMENT WITH THYROID AND MERCURY. W. A. STARKER, München. med. Wchnschr. **78**:709 (April 24) 1931.

Starker reports a case of combined myxedema and congenital syphilis in a girl 10 years old whom he treated with thyroid and daily mercurial inunctions. In a month there was marked mental and physical improvement.

BRAHDY, Mount Vernon, N. Y.

THE VARIABILITY OF THE VIRULENCE OF TUBERCLE BACILLI. H. J. TIEDEMANN, München. med. Wchnschr. **78**:908 (May 29) 1931.

The virulence of tubercle bacilli is not always fixed. Tiedemann refers to one bovine strain which was transplanted for twenty-five years and was much less virulent for animals at that time than originally. Glycerin-potato and glycerin-

bile-potato mediums have been used for attenuating the virulence of tubercle bacilli. The virulence of some strains of tubercle bacilli can be increased by repeated passages through animals.

BRAHDY, Mount Vernon, N. Y.

HISTOLOGY OF LESIONS CAUSED BY THE CALMETTE AVIRULENT (B C G) TUBERCLE BACILLUS. C. SCHILLING, Virchows Arch. f. path. Anat. **278**:462, 1930.

Guinea-pigs were inoculated intravenously or intracardially with the Calmette bacilli and killed at intervals of from seven to sixty-one days. One animal of each series was superinfected with a virulent strain of human tubercle bacillus fourteen days after the primary inoculation in one instance and forty-seven days in the other instances. In each series, animals were infected with the virulent strain without previous inoculation of the avirulent strain. The Calmette organisms localize in the lungs and multiply with the formation of dense bacillary clumps, in which the bacilli in time lose their acid-fast property. They evoke the formation of minute lesions grossly like typical miliary tubercles. These are composed of endothelioid cells, with an outer zone of fibroblasts. The lesion is infiltrated by polymorphonuclear leukocytes, many of which undergo degeneration. Lymphocytic infiltration is inconspicuous. Typical Langhans' giant cells are only occasionally formed, and caseation necrosis does not occur. The lesions become encapsulated by connective tissue and may finally disappear without leaving a trace. The organism may not be considered wholly avirulent, since it is able to multiply in the tissues and to evoke a tissue reaction in which necrosis of leukocytes occurs. In animals superinfected with virulent tubercle bacilli, typical tubercles were not formed, and multiplication of the injected bacilli could not be detected. Schilling concludes that there can be no question of the antigenic action of the Calmette bacillus against virulent bacilli.

SCHULTZ, Chicago. [ARCH. PATH.]

THE INFLUENCE OF THE VEGETATIVE NERVOUS SYSTEM IN TUBERCULOUS MENINGITIS IN CHILDREN. P. S. MEDOWIKOV and D. O. SCHENKMAN, Ztschr. f. Kinderh. **52**:325 (Feb.) 1932.

The blood pressure and pulse rate after injection of epinephrine hydrochloride were studied in thirty children with tuberculous meningitis and two with serous meningitis. In children with the serous type the blood pressure and pulse rate rose, while in those with the tuberculous type there was a drop. The authors conclude that children shortly before they succumb to tuberculous meningitis are vagotropic.

D. H. SHELLING, Baltimore.

THE TREATMENT OF TUBERCULOSIS OF THE SKIN BY THE GERSON-HERRMANNSDORFER-SAUERBRUCH DIET. E. BRUUGSGAARD and E. HVAL, Norsk mag. f. lægevidensk. **92**:1157 (Nov.) 1931.

The Gerson-Herrmannsdorfer-Sauerbruch diet was used for seventy-five patients with tuberculosis of the skin; sixty-two of these patients had lupus vulgaris. For most of the patients the diet alone was used; for some the diet was combined with the use of Finsen light. In the majority of cases a cure took place; only a few patients were unaffected by the treatment. The diet, combined with the use of Finsen light, gave the best results; the authors predict that this will be the treatment of the future.

Besides causing the cutaneous lesions to subside, the diet proved to have an excellent effect on the general health of the patient. Positive cultures of tubercle bacilli could be found until the tuberculous infiltrate was completely absorbed; then only scar-tissue was left. Thus the diet does not seem to act through formation of specific antituberculous substances in the skin but rather by raising the resistance of the patient to the tubercle bacilli.

An outstanding feature in the effect of the diet is the tissue-absorbing action. The sclerotic connective tissue and the lupus infiltration are quickly absorbed, even when the lupus infiltration is embedded in masses of hypertrophic scar tissue. In this way otherwise intractable patients are rendered accessible to an effective curative treatment.

TOVERUD, Oslo, Norway.

Internal Diseases

CONGENITAL MEDIAL SCLEROSIS OF THE CORONARY ARTERY. R. W. KISSANE and R. S. FIDLER, Am. Heart J. **7**:133 (Dec.) 1931.

The authors describe a case occurring in an infant who died at the age of 3 days, following intermittent attacks of cyanosis and apnea, during which oxygen and artificial respiration were employed. Previous to death there was marked cyanosis. The pulse rate was 140. There was some cardiac enlargement. At autopsy an unusual degree of coronary prominence was noted. The coronaries were quite firm, cordlike and opaque. No other abnormalities were found. An extensive pathologic discussion then follows. Other cases have been previously described by McMicheal (a child aged 18 months), Hughes and Perry (a child aged 7 weeks), Surbek (a child aged 3 days) and Jaffe (a child aged 2 days).

BACHMANN, Chicago.

RHEUMATIC HEART DISEASE: INCIDENCE AND ROLE IN THE CAUSATION OF DEATH (A STUDY OF 5,215 CONSECUTIVE NECROPSIES). DAVID DAVIS and SOMA WEISS, Am. Heart J. **7**:146 (Dec.) 1931.

The authors report the results of an intensive study of 5,215 necropsy records from the Boston City Hospital. Age groups are not included, so that no direct pediatric value is obtained. Some points of interest may, however, be gleaned from the report: 1. The high incidence of rheumatic heart disease reported makes rheumatic fever a rather prevalent disease, comparable to carcinoma. The study revealed rheumatic disease of the heart in 9.1 per cent of the cases. 2. Rheumatic disease of the heart was found to be slightly more prevalent among females. 3. In the entire series there were 47 cases of subacute bacterial endocarditis. Of these, 35 gave evidence of a previous rheumatic infection in the form of a definite old rheumatic endocarditis discovered by gross examination or from a characteristic clinical course.

BACHMANN, Chicago.

THE INCIDENCE OF HEART DISEASE AND OF THE ETIOLOGICAL TYPES IN A SOUTHERN DISPENSARY. EDWARD H. SCHWAB and VICTOR E. SCHULZE, Am. Heart J. **7**:223 (Dec.) 1931.

The authors report a study of the incidence of heart disease in a southern dispensary. In this excellent report there is one paragraph of real pediatric interest. The number of patients included in this series suffering with a rheumatic type of heart disease is too small to justify arrival at any conclusion as regards the influence of race or sex on the incidence of this etiologic type. The low incidence of rheumatic heart disease in this community is readily explainable on the basis of the rare occurrence of the rheumatic series of infections in the south, a phenomenon in which climate appears to play a large part.

BACHMANN, Chicago.

BRONCHIAL OBSTRUCTION: ITS RELATION TO ATELECTASIS, BRONCHOPNEUMONIA AND LOBAR PNEUMONIA. P. N. CORYLLOS AND G. L. BIRNBAUM, Am. J. Roentgenol. **22**:401 (Nov.) 1929.

The authors consider atelectasis, generally postoperative apneumatosis, bronchopneumonia and lobar pneumonia of a common pathogenesis, that is, secondary to

bronchial obstruction and depending only on the type or virulence of the organism present. Pneumococcic atelectasis or pneumococcic bronchial obstruction is suggested for the designation of lobar pneumonia. In pneumonia, as in atelectasis, the size of the bronchus obstructed varies with the viscosity of the exudate and the degree of edema of the mucosa, so that massive lobar or lobular atelectasis or pneumonia may result. Bacillus influenzae, the staphylococcus and the streptococcus, which produce a less viscid exudate, are more apt to produce pneumonia. Among the objections to this theory are the frequent absence of bronchial obstruction at autopsy in atelectasis and in lobar pneumonia, the frequent absence of displacement of the trachea and heart in pneumonia, the great difference in prognosis and toxicity and the frequent absence of a preceding bronchitis in pneumonia. The evolution of the disease syndrome is represented by: bronchitis—atelectasis—pneumonia. Photomicrographs, roentgenograms and photographs of gross specimens are shown with endoscopic observations, symptoms and signs to show the similarity in pathogenesis and the differences in local and general changes. Rational treatment should aim to reestablish free drainage of the bronchial tree. Inhalations of from 5 to 10 per cent carbon dioxide seem to possess a specific action against pneumococcic pulmonary infections, and, according to experimental and clinical data, should be used both as a preventive and as a curative agent. A voluminous bibliography is included.

STULIK, Chicago.

"SPOTTED BONES." WILLIAM S. NEWCOMET, Am. J. Roentgenol. **22**:460 (Nov.) 1929.

Osteopoikilosis or disseminated condensing osteopathy, in which a spotting or condensation of practically all the bones is found, is symptomless and the diagnosis is made accidentally after roentgen examination. Of the few cases reported the youngest was that of a boy aged 14 years. It evidently must be associated with some change in certain cartilaginous structures in early life, its distribution being confined to that portion of the bone. Unlike exostoses, which are also painless, it does not appear on the shaft of the long bones or on the head.

STULIK, Chicago.

OSTEITIS FIBROSA AND ALLIED DISEASES OF BONE (THE OSSEOUS DYSTROPHIES). L. H. GARLAND, Am. J. Roentgenol. **22**:517 (Dec.) 1929.

When porosis predominates, osteodystrophia fibrosa may be of the following types: when generalized, osteitis fibrosa cystica (von Recklinghausen); when localized, multilocular bone cysts, epulis or leontiasis ossea, or when circumscribed, solitary bone cysts or central "fibromas." When hyperostosis predominates, generalized osteitis deformans (Paget) or localized monosteal osteitis deformans may occur. These conditions bear some relation to rickets and osteomalacia, and the etiology of both groups is obscure. The theories of diet, metabolism, endocrines, vitamins, calcium and hormones are discussed. Thirteen case reports illustrating various forms of osseous dystrophies are presented, together with roentgenograms and the differential diagnosis. A bibliography is appended.

STULIK, Chicago.

ROENTGEN IRRADIATION IN UNRESOLVED PNEUMONIA. EDWIN A. MERRITT and EDGAR M. MCPEAK, Am. J. Roentgenol. **23**:45 (Jan.) 1930.

Of seven cases of unresolved pneumonia in which roentgen irradiation was employed, four cleared up entirely, two showed definite improvement and one was unchanged. The four cases responding to treatment were those in which the process involved the parenchyma only, which would seem to show that resolution is brought about more quickly in this type of case. In the two cases showing improvement the process involved the glands of the hilus, and in one of these

there was also an area of infiltration in the parenchyma, which responded rapidly. Lesions of the hilus seem more sluggish in their response and require more therapy than those involving the parenchyma alone. The case that did not respond was that of an old man of 70 with a chronic lesion of over a year's duration. Treatment is suggested for cases showing definite roentgen signs of delayed resolution three weeks after onset.

STULIK, Chicago.

HISTOPLASMOSIS (DARLING) WITHOUT SPLENOMEGALY. R. M. CRUMRINE and JOHN F. KESSEL, Am. J. Trop. Med. **11**:435 (Nov.) 1931.

The authors report a case of histoplasmosis (Darling) without splenomegaly in a mulatto, with the autopsy record, and give a brief review of the literature on this condition. The early death of this patient was thought to be the possible explanation for the absence of splenomegaly. The authors also report, in addition to the intracellular phase, a second or extracellular phase in which the organism is surrounded by a halo or capsule of considerable thickness. This is the fifth case of this condition reported in the literature.

BURPEE, Augusta, Ga.

AMEBIASIS. WILLIAM E. MUSGRAVE, Am. J. Trop. Med. **11**:469 (Nov.) 1931.

The author gives a review of amebiasis based on a clinical study of 20,000 cases and 3,000 autopsy records extending over a period of twenty years. The etiology, pathology, symptomatology, complications, sequelae, diagnosis and prophylaxis are discussed at length. Special attention is given to the symptomatology in the mild and unusual cases and complications in the larger bowel. In children the author found the disease to be less frequent and to run a milder course, sometimes terminating in recovery without treatment. Complications were exceedingly rare in patients receiving appropriate treatment.

BURPEE, Augusta, Ga.

MYATONIC CARDIAC MURMURS. J. EPSTEIN, Arch. Pediat. **48**:635 (Oct.) 1931.

"A murmur is frequently heard in children and young adults which cannot be traced to embryological cardiac malformation, endocardial valvular deformity, myocardial disease, pericardial adhesions, hypertension, or changes in the blood. Because of its uncertain etiology it has received many names which are used carelessly and interchangeably. The uncertainty in the origin of this murmur has also led to its being either totally disregarded or too seriously evaluated. It is therefore of considerable importance for theoretical as well as for practical reasons to put this murmur on a scientific basis.

"From a study of 20 children with this oft-heard murmur, it is evident that the murmur is caused by a lack of cardiac tonicity due to a muscular or vagus hypofunction. In some cases, the murmur probably originates in the papillary muscles. Cardiac atonia or myatonia may be congenital or acquired. A relaxed heart will be unduly and unequally stretched by the sudden intraventricular impact of blood during systole and give rise to abnormal vibratory movements and to a murmur. Since the origin of this murmur may be traced to a defective cardiomuscular tonicity, the murmur condition may be properly called myatonia cordis and the murmur itself myatonic murmur. The term myatonic murmur will replace a group of unscientific and misleading names.

"The diagnosis is based on the fact that the murmur is an isolated phenomenon, in a heart of normal size, and in a patient who has no subjective or objective cardiac disorders. The prognosis is generally good, but there is always an element of uncertainty, because a perfectly normal heart does not murmur. The treatment is that of the patient and not of the heart."

AUTHOR'S SUMMARY.

PREMATURE CONTRACTIONS OF THE HEART IN CHILDREN. L. ANTELL, Arch. Pediat. **48**:640 (Oct.) 1931.

Three cases of premature contractions of the heart are reported. The physiology of the heart is reviewed briefly, as well as some of the confusing literature on this subject. The author believes that in the absence of signs of cardiac damage, the history of the case should help in the diagnosis and treatment. He stresses the importance of cardiac enlargement even though it is slight.

WADDELL, University, Va.

A CASE OF CRETINISM THIRTY-ONE YEARS UNDER OBSERVATION. CHARLES GILMORE KERLEY, Arch. Pediat. **48**:668 (Oct.) 1931.

A case of cretinism that was under observation for thirty-one years is reported. The interesting feature of the case is the wide difference in the amount of thyroid substance required at the different ages. During the developmental period of childhood and early womanhood large doses were necessary.

WADDELL, University, Va.

VACCINE TREATMENT OF ASTHMA IN CHILDHOOD. A. GRAEME MITCHELL and MERLIN L. COOPER, Arch. Pediat. **48**:751 (Dec.) 1931.

The present conceptions of asthma as it occurs in childhood are discussed, particularly asthma associated with infection of the upper respiratory tract. Literature having to do with vaccinotherapy is reviewed, and the authors report their results in eleven patients treated with autogenous vaccines. Cultures were taken from the nose and throat during an attack of acute infection of the upper respiratory tract. Skin sensitivity to the various organisms obtained was determined and a mixed vaccine made from the organisms to which the patient appeared sensitive. "In treatment, one-half to one minim was injected subcutaneously and, depending upon the degree of local reaction which should not be too severe or last more than 24 hours, this dose was repeated and increased daily until a maximum of eight minims was reached, upon which this amount was given two or three times a week for several weeks longer." Improvement appeared to follow this method of therapy, and while drawing no conclusions from a small series of cases the authors are of the opinion that certain children whose asthmatic attacks are associated with infections of the upper respiratory tract are decidedly benefited by vaccines. In some instances attacks that previously were frequent ceased for months or years following this method of therapy. Attention is called to the fact that it may be necessary to repeat the treatment with freshly prepared vaccine after a period of several months.

WADDELL, JR., University, Va.

OBSTRUCTION OF PYLORUS IN INFANCY. A. A. CONRAD, Nebraska M. J. **17**:49 (Feb.) 1932.

The author reviews the history, etiology, pathology and symptomatology of obstruction of the pylorus in infancy, and presents the record of a patient who began to vomit on the second day of life. The condition was controlled by the use of atropine and phenobarbital. He recommends that atropine be given in increasing doses to a physiologic effect in pylorospasm.

HAMILTON, Omaha.

THE ELECTROCARDIOGRAM OF NORMAL SCHOOL CHILDREN. C. BRUCE PERRY, Arch. Dis. Childhood **6**:259 (Oct.) 1931.

In this study, school children with normal hearts clinically were examined with the electrocardiograph; 100 children, 50 boys and 50 girls, were selected. The electrocardiograms were made in the sitting position, with nonpolarizable

immersion electrodes and the galvanometer standardized, so that 1 millevolt gave a deflection of 10 mm. The conclusions from the study were: 1. The incidence of sinus arrhythmia varies inversely with the rate of the heart. Other types of arrhythmia are rare in childhood. 2. The P-R interval tends to be shorter in children than in adults. 3. The Q-R-S complex may be notched or splintered in lead III with no clinical significance. 4. This is frequently associated with inversion of T in lead III, which occurs with such great frequency (54 per cent) as to be almost the normal finding. 5. Splintering of Q-R-S and inversion of the T wave do not occur normally in children except in lead III. 6. There is no significant age change or sex difference in the electrocardiogram of children between the ages of 5 and 14 years.

KELLY, Milwaukee.

CONGENITAL ANOMALIES OF THE HEART IN ELEMENTARY SCHOOL CHILDREN. C. BRUCE PERRY, Arch. Dis. Childhood **6**:265 (Oct.) 1931.

In examinations of a number of school children referred for cardiac conditions, 119 were found to have various constant physical signs suggestive of congenital cardiac lesions. These cases were studied and classified, according to physical signs, into six groups. Roentgenograms of the chest were of no great help in diagnosis, other than in revealing more or less cardiac enlargement than was expected clinically. Electrocardiography was of no value in differentiating between these minor congenital abnormalities of the heart.

KELLY, Milwaukee.

THE VALUE OF ALKALI IN SALICYLATE THERAPY. NOAH MORRIS and STANLEY GRAHAM, Arch. Dis. Childhood **6**:273 (Oct.) 1931.

The oral administration of sodium salicylate alone in doses over 60 grains (3.88 Gm.) daily to children results in salicylate poisoning. Vomiting, a confused mental state, air hunger, a fall in the carbon dioxide content of the blood and albuminuria are noted if the dosage is increased to 90 grains (5.83 Gm.) for several days. The administration of equal or larger doses of alkali prevents the symptoms of salicylate poisoning. This effect may be due to the prevention of renal damage, thus permitting more rapid excretion of salicylate.

KELLY, Milwaukee.

DWARFISM WITH STIPPLED EPIPHYSES. W. GORDON SEARS, Brit. J. Child. Dis. **28**:290 (Oct.-Dec.) 1931.

The author describes the case of a youth, aged 19 years, who was undersized and had the general appearance of a child of 8 or 9. He had slight lordosis but good muscular development. He was mentally retarded, was 48 inches (121.9 cm.) high and weighed 61 pounds (27.6 Kg.). The upper and lower extremities were shortened. The roentgenograms showed delayed and irregular ossification of the heads of the femora and patellae; also delay in the union of the iliac centers with the ischial and pubic portions of the pelvis. The ossification of the iliac crests was irregular, and the heads of the femora were flattened and showed a number of irregular areas of ossification. Also fine transverse striations of the diaphysis of the femora and tibiae at their growing ends were noticed. Nothing is definitely known about the etiology of these cases.

LANGMANN, New York.

A NEW THEORY OF THE MECHANISM OF U-V IRRADIATION IN RHEUMATIC DISEASES. LLEWELLYN JONES LLEWELLYN and A. BASSETT JONES, Brit. J. Phys. Med. **6**:181 (Dec.) 1931.

The authors believe that rheumatism is primarily the outcome of an inborn tendency toward instability of the heat or temperature regulating mechanism, and

they denounce the fact that "we with 'damnable iteration' pay servile homage to one factor only: Infection—et praeterea nihil." The facts and deductions are briefly these: Tyrosine is the mother substance of which the temperature-regulating hormones, thyroxine and epinephrine, are chemical derivatives and from which melanin is formed through the action of the ferment tyrosinase. Tyrosine enters into the formation of insulin, another heat-producing hormone. The sulphur content of insulin is derived from cystine. Tyrosine and cystine are stored in the skin. The blood content of both amino-acids, and hence potentially of thyroxine and epinephrine, is increased by ultraviolet irradiation. Ultraviolet irradiation should prove an invaluable adjunct in both the prevention and the treatment of rheumatism.

HARTMAN, Cleveland.

TREATMENT OF THE ASTHMATIC BY PHYSICAL EXERCISES. A. H. DOUTHWAITE, Brit. J. Phys. Med. **6**:190 (Dec.) 1931.

The author outlines in detail exercises to combat the abnormal bodily changes of the asthmatic patient. Specific measures are described for maintaining general muscular relaxation. Exercises are outlined for the prevention and treatment of thoracic rigidity and for the reduction of pulmonary distention.

HARTMAN, Cleveland.

FEBRILE ATTACKS. WILFRED ATTLEE, Practitioner **128**:13 (Jan.) 1932.

In considering this common problem, the author confines his observation mainly to the febrile attacks occurring in boys in boarding schools. He considers that fever in adolescence takes the place of vomiting and convulsions in infancy. He divides the attacks into two types: those occurring singly and those occurring in groups. He states that the isolated febrile attacks are usually not of infectious origin, whereas the second group is always contagious. Accurate diagnosis is mainly a problem of complete physical examination. The author stresses the need for testing flexion of the neck as a routine measure, and also says that urinalysis should be carried out in all cases. When fever persists for several days and a diagnosis has not been made, some of the more unusual conditions must be considered: Bacillus coli infection of the urinary tract, pyemia, acute rheumatism, tuberculosis and the enteric fever group. Under treatment, Attlee states: "The backbone is mainly to rely upon rest, fluids and a mild antipyretic." Rest during convalescence is of paramount importance.

SAPPINGTON, San Francisco.

STILL'S DISEASE AND RHEUMATOID ARTHRITIS. RUPERT WATERHOUSE, Proc. Roy. Soc. Med. **24**:1607 (Oct.) 1931.

In 1896, Still published a description of a form of chronic disease of the joints in children which has since been known by his name. He summed up his conclusions as follows: This disease begins before the second dentition, and is characterized clinically by elastic fusiform enlargement of the joints without any bony change and also by enlargement of the glands and spleen. This disease has hitherto been called rheumatoid arthritis, but it differs from that disease in adults clinically in the absence of bony change and in the enlargement of the glands and spleen, and pathologically in the absence of cartilaginous changes and also in the absence of osteophytic change. Still employed the term "rheumatoid arthritis" as a synonym for osteo-arthritis and what is known in America today as hypertrophic as opposed to atrophic or infective arthritis. The author collected seventeen cases in which the onset of disease was during the first seven years of life. He records the differences in children and adults in attacks of rheumatoid arthritis.

WILLIAMSON, New Orleans.

PERSISTENT HAEMATURIA. R. G. WALLER, Proc. Roy. Soc. Med. **25**:143 (Dec.) 1931.

A patient, aged 2¼ years, was admitted to the hospital with a history of hematuria for four days. There were also left-sided otorrhea and mastoiditis. The mastoid was opened and drained, and cultures from the pus showed streptococci. Three cubic centimeters of antistreptococcic serum was given. The wound healed and the general condition was much improved, but the hematuria continued. Roentgenograms of the kidneys showed no abnormality. The urine showed albumin, a copious deposit of red cells and an excess of leukocytes.

WILLIAMSON, New Orleans.

GASTROSCOPIC OBSERVATIONS IN CHRONIC GASTRITIS. R. SCHINDLER, Arch. d. mal. de l'app. digestif **21**:680 (June) 1931.

Schindler states that gastroscopy is the only method by which a diagnosis of chronic gastritis can be made certain. Macroscopic inspection of a mucous surface is the surest method of making a diagnosis of its chronic inflammation. With the gastroscope the image is exact and the colors "appear in brilliant splendor." The author states that gastrophotography will not be considered seriously as a diagnostic method. He describes the images seen with the gastroscope in various diseases. No description of the apparatus itself is given.

TURNER, Chicago.

PATHOGENESIS OF LIPOID NEPHROSIS: ITS CONNECTION WITH THE STATE OF THE THYROID GLAND. E. COELHO and J. ROCHETA, Presse méd. **39**:1875 (Dec. 19) 1931.

Lipoid nephrosis is the name given to a rare clinical entity characterized by hypercholesteremia, hypoproteinemia, inversion of the serum-globulin ratio, marked albuminuria and birefracting lipoids in the urine. There is generalized edema but no hematuria or rise in blood pressure. A number of investigators hold that a deficiency in thyroid secretion may be responsible for this syndrome. The authors, however, found no improvement in their cases as the result of thyroid administration, and were unable to produce the syndrome experimentally in dogs by means of thyroidectomy. They conclude that lipoid nephrosis is a disease primarily metabolic, secondarily renal, having in its pathogenesis no connection with the state of the thyroid gland.

BIEKER, St. Petersburg, Fla.

HEPATIC FORM OF INFANTILE KALA-AZAR. ROBERT POINSO, Presse méd. **39**:1920 (Dec. 30) 1931.

A rare form of infantile kala-azar is described by Poinso, and two cases are reported. Instead of the usual findings, in these cases there was tremendous enlargement of the liver, with only moderate splenic enlargement. The differential diagnosis with this reversal of objective symptoms is important but not difficult. Tuberculosis, syphilis and Malta fever may present the same findings, but the geography, irregular fever, enlargement of the liver for several months with concomitant splenic enlargement, anemia, surroundings and presence of dogs in the immediate neighborhood are highly suggestive. Splenic puncture is important, for the presence of Donovan bodies in the juice confirms the diagnosis. The prognosis in the hepatic form is apparently the same as that in the splenic form. Treatment with antimony gives good results. The possibility of Leishmania as a cause of infantile cirrhosis must be considered.

BIEKER, St. Petersburg, Fla.

PURULENT ASEPTIC PLEURISY IN THE COURSE OF PNEUMONIA AND BRONCHOPNEUMONIA IN INFANTS. R. STANKIEWICZ, Rev. franç. de pédiat. **7**:629 (Oct.) 1931.

In pulmonary congestion due to pneumonia or bronchopneumonia the pleura is usually involved in children up to 3 years of age. Nine per cent of these cases show a purulent nontuberculous pleurisy. The origin of these nontuberculous forms is apparently in the pneumonia process itself. The recognition of this complication is important from the standpoint of prognosis.

SANFORD, Chicago.

THERAPY OF INFANTILE LEISHMANIOSIS. C. BALDI, Prat. pediat. **9**:189 (May) 1931.

A 3 year old child presented the typical clinical picture of infantile leishmaniosis, the diagnosis being confirmed by the finding of the parasites in the bone marrow, by puncture. The child was treated intravenously with an antimony preparation for forty days, receiving a quantity of antimony equivalent to 45 cc. of the tartrate. In this time there was no improvement, but, following four irradiations, a second course of the antimony preparation resulted in an almost critical cessation of the disease.

DOOLEY, Kent, Conn.

ANEMIA OF INFANTS. T. GUGLIELMINI, Prat. pediat. **9**:235 (June) 1931.

The author reviews the subject of the anemia of infants briefly without making any original contribution.

DOOLEY, Kent, Conn.

CONGENITAL STENOSIS OF THE CARDIAC AND PYLORIC ORIFICES. D. GIORDANO, Prat. pediat. **9**:515 (Dec.) 1931.

A 2 year old child was seen because she was thought to have swallowed a button. Roentgenograms taken while the child was in the upright position showed the opaque meal arrested in a dilated esophagus. However, when films were taken of the child in the horizontal position, the meal was found to have escaped into the stomach and to be arrested there. At operation, stenosis of both the cardiac and pyloric regions was discovered and corrected. Roentgenograms taken three weeks after operation showed the obstruction to be satisfactorily relieved.

DOOLEY, Kent, Conn.

MEDICAL TREATMENT FOR PNEUMOCOCCUS EMPYEMA IN CHILDREN. C. ARTUSI, Riv. di clin. pediat. **29**:724 (Sept.) 1931.

This article of forty-eight pages is devoted to extensive reports of seventeen cases of pneumococcus empyema at the Pediatric Clinic in Bologna. The method of treatment described by Cocchi (*Riv. di clin. pediat.* **25**:410, 1927; abstr., AM. J. DIS. CHILD. **34**:673 [Oct.] 1927) was followed: evacuation of the pus by means of an aspirating needle and syringe, washing of the pleura with physiologic solution of sodium chloride and then introduction of a solution of sodium taurocholate (from 1 to 3 Gm.). Of the seventeen children between 1 and 12 years, one aged 12 months died; the others were completely cured in a relatively short time. In four of these, rib resection was eventually resorted to. The evacuation of the pus and the lavage of the pleura did not disturb the patients much. In only two of the eighty-one thoracenteses was it necessary to resort to ethyl chloride anesthesia. The sodium taurocholate was tolerated well in doses even larger than those used by Cocchi. In six cases a pneumothorax developed, which, however, did not unfavorably influence the course and duration of the illness. The conclusions drawn are: "We maintain that in all empyema cases from pneumococci, one should first try medical treatment, especially in the parapneumonic cases with

much fluid pus and in small children. In a majority of cases, this treatment is sufficient to obtain a cure in from one to two months. Secondary rib resection in the more obstinate cases of empyema is much less dangerous than early operation, and in our patients always resulted in a cure."

HIGGINS, Boston.

THE ANAPHYLACTIC BRONCHIAL ASTHMA OF CHILDREN. LINA VIOLA, Riv. di clin. pediat. **29**:772 (Sept. 15) 1931.

In twenty-nine babies and children with asthma, the ordinary protein tests were negative, except in two who reacted to an extract of Aspergillus niger.

HIGGINS, Boston.

THE AMOUNT OF NONPROTEIN NITROGEN IN THE BLOOD OF CHILDREN: II. NEPHROSIS AND NEPHRITIS; ENTEROPATHY AND DISTURBANCES OF NUTRITION; SPASMOPHILIA. A. PICCIOLI, Riv. di clin. pediat. **29**:819 (Oct.) 1931.

The micromethods of Bang were used in determining the total nonprotein nitrogen, urea nitrogen and amino-acid nitrogen of the blood. Six children with renal disturbances, eight with acute enteritis and four with tetany were studied, observations being made on the blood of each child for several days. In children with nephrosis, the nitrogen of the blood is not increased, although in hemorrhagic nephritis and pyelonephritis there may be a moderate azotemia. In each case of acute enteritis, an abnormal increase in the nitrogen of the blood was observed.

In tetany, there was also a hyperazotemia in each case. The increase over normal was more marked in patients with active than in those with latent tetany. This observation may prove of diagnostic value.

HIGGINS, Boston.

CELIAC DISEASE. V. ROSSI and G. SANNA, Riv. di clin. pediat. **29**:874 (Oct.) 1931.

The authors report the case of a boy aged 18 months with celiac disease. In celiac disease there may be various etiologic factors; in this case, a hereditary factor seemed to predominate. The mother had a goiter, and a brother died at 29 months of age of a disease very similar to that of the patient. The patient showed a marked sympathetic hypotonia.

HIGGINS, Boston.

SPONTANEOUS PNEUMOTHORAX OF NONTUBERCULOUS ORIGIN IN INFANCY. M. ACUÑA, S. I. BETTINOTTI and M. T. VALLINO, Arch. argent. de pediat. **2**:349 (July) 1931.

The authors present a schematic outline of the etiology, symptomatology, diagnosis, prognosis and treatment of spontaneous nontuberculous pneumothorax in infancy. They further present a report of four clinical cases with corresponding roentgenograms. Case 1: An infant aged 3 months had a pulmonary abscess, followed by a suddenly developing pyopneumothorax; death ensued. Case 2: In an infant aged 15 months, spontaneous pneumothorax developed in the course of a nontuberculous pleuritis, with severe paroxysms of coughing. Recovery took place in two months. Case 3: In an infant aged 5 months, otitis media occurred with multiple pulmonary abscesses, followed by the sudden development of pyopneumothorax; death took place several hours later. Case 4: In an infant aged 7 months, a spontaneous pneumothorax developed insidiously, following bronchopneumonia. Recovery occurred in two months. The authors comment that pyopneumothorax is almost always fatal, while simple noncomplicated pneumothorax is frequently followed by recovery.

SCHLUTZ, Chicago.

OSTEOPSATHRYOSIS. JOSÉ SYMON and RAUL ORTEGA, Arch. hosp. de niños **2**:41 (March) 1931.

The authors report the case of a family in which a paternal aunt and the father suffered from osteopsathyrosis. The father was married to a healthy wife with whom he had seven children. Two of these presented typical cases of osteopsathyrosis and another had some of the stigmas; all the others were completely free from the disorder.

SCHLUTZ, Chicago.

THE AVERAGE BLOOD PRESSURE IN THE NORMAL INFANT AND IN SOME PATHOLOGIC STATES. JOSÉ BONABA and ALEJANDRO SARACHAGA, Arch. de pediat. d. Uruguay **2**:567 (Dec.) 1931.

The average blood pressure in the normal child has a fixed value, and between the ages of 1 and 14 years varies hardly more than a centimeter in either direction. In the sick infant the average blood pressure is always elevated in acute nephritis and lowered in typhoid fever.

SCHLUTZ, Chicago.

ROUNDED SHADOWS IN THE THORAX: A ROENTGEN STUDY. JUAN JOSÉ BERETERVIDE, Rev. méd. latino-am. **16**:1561 (Aug.) 1931.

The author points out the importance of the roentgen interpretation of round opacities in the thorax. Since the pandemic of grip from 1918 to 1921 there has been an increase in suppurative processes and primary neoplasms in the lungs. According to Peuteuil, opacities produced by lesions that arise in the parenchyma of the lung are usually spherical and rounded, owing to the physical conditions that intervene. The author analyzes in detail the characteristics, such as the number (whether single or multiple), the location, the size, the relation to the mediastinum, the symptoms and the associated lesions, of various tumors and cysts occurring in the thoracic cavity. Of particular interest is his account of a dermoid cyst of pleural origin.

DWYER, Kansas City, Mo.

THE GLYCEMIC REACTION TO EPINEPHRINE IN HEPATIC CIRRHOSIS. LORENZO GALINDEZ, FIDEL A. MACREL CRESPO, FRANCISCO R. D'OVIDIO and IRMA COLON, Rev. méd. latino-am. **16**:1611 (Aug.) 1931.

The authors have not obtained the paradoxical postepinephrine hypoglycemia described by Larsitano in cases of atrophic and hypertrophic cirrhosis that they have studied. They believe that in atrophic cirrhosis, in spite of the diminished relative quantity of glycogen in the liver, there is always a mobilization after epinephrine and, consequently, more or less obvious hyperglycemia. As to the hyperinsulinism produced by epinephrine, which should be partially the cause of the paradoxical hypoglycemia, the authors believe that it is questionable that in the cirrhosis of Laennec, in which the pancreas and at the same time the acini also show sclerosis, the cells of Langerhans are affected.

DWYER, Kansas City, Mo.

CHONDROFIBROMA OF THE ABDOMINAL WALL. OSCAR J. CAMES and JOSÉ M. CED, Rev. méd. latino-am. **16**:1646 (Aug.) 1931.

The authors observed a patient with a chondrofibroma in the wall of the abdomen at the external border of the rectus muscle in the region of the left flank. It had appeared a year previously and had attained the size of a pigeon's egg. Histologic examination revealed a chondrofibromatous structure, as the photomicrographs show which accompany this work.

DWYER, Kansas City, Mo.

THE PROGNOSIS OF SEROUS EXUDATIVE PLEURITIS. D. OROSZ, Arch. f. Kinderh. **95**:1, 1931.

The present study was based on cases of pleurisy with effusion seen in the Kinderklinik at Vienna from 1923 to 1929. Of 130 cases, 119 were on a tuberculous basis and in 67 of these the patients were reexamined from two to eight years after the time of the effusion. Physical examinations were checked with roentgenologic studies. Of the 67 patients, 26 were entirely normal, 28 showed insignificant changes, 5 showed moderately severe changes, 5 had severe lung and bone changes and 3 died of tuberculosis. Three of those showing severe changes and the three who died had shown considerable involvement of the lung parenchyma at the time of the first examination. Among 8 infants and small children only 1 death occurred in six years. The prognosis of serous exudative pleuritis in infants and children is thus fairly good at all ages. No relationship was noted between the size of the effusion and the prognosis.

LESLIE, Evanston, Ill.

A CASE OF CONGENITAL PORPHYRINURIA. H. T. SCHREUS and C. CARRIÉ, Dermat. Ztschr. **62**:347 (Dec.) 1931.

The patient was a laborer, aged 20, whose sister had suffered with a similar disease and had died at the age of 32. The condition started in the patient at the age of 5, and consisted of the development of bullae on areas exposed to the sun. These bullae healed, leaving scars. The season had no influence on the development of lesions, except that there were more in the summer. Trauma of previously affected areas caused the formation of bullae. Physical examination gave normal results, except for an increase of the porphyrin in the urine. Exposed portions of the skin showed marked scarring, pigmentation and areas of depigmentation. Tests for liver function showed no abnormality. The condition is differentiated from hydroa vacciniforme in that there is no increase of porphyrin in the urine in the latter disease. Histologic study and experiments with artificial ultraviolet light were carried out. The blood serum, bullae and follicles of the skin showed a red fluorescence under the rays of a Kromayer lamp filtered through a piece of "Wood" glass.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

UNDULANT FEVER IN CHILDHOOD. JULIUS BAUER, Kinderärztl. Praxis **2**:150 (April) 1931.

The author reports a case of undulant fever in a 14 year old boy, and discusses the symptoms.

HUENEKENS, Minneapolis.

LYMPHOID GLAND FEVER. E. JAKOBSOHN, Med. Klin. **27**:1145 (July 31) 1931.

Two cases of so-called lymphoid gland fever are described. Both are characterized by an enlargement of the lymph nodes and the spleen and relative lymphocytosis. The etiology is obscure. No specific treatment is known. The prognosis is good.

ZENTAY, St. Louis.

LACTIC ACID MILK IN ANEMIA OF INFANCY. GEORG BISCHOFF, Monatschr. f. Kinderh. **51**:174 (Oct. 31) 1931.

Since 1912 a one-sided diet of milk has been supposed to lead to anemia in infants. This observation has been made by Finkelstein, Czerny, Pfaundler and others. For four years, lactic acid milk has been used in the children's clinic of Göttingen. As such feeding necessitates a diet containing all the elements of milk, the author wondered whether this feeding predisposed to anemia. He found that lactic acid milk behaves in a general way like whole milk. Iron and the usual

accessories, such as arsenic and vitamins, must be used. Lactic acid milk does not hinder regeneration of the blood, and has proved satisfactory as a permanent food.

GERSTLEY, Chicago.

THE SIGNIFICANCE OF CONSTITUTION IN LYMPHATIC LEUKEMIA. VALERIE DEUTSCH, Monatschr. f. Kinderh. **51**:280 (Nov.) 1931.

Lymphatic leukemia is characterized by universal swelling of the lymph nodes, fever, severe malaise, pain in the bones, an enlarged spleen, a hemorrhagic diathesis, ulcerations in the mouth, anemia, thrombopenia and characteristic changes in the white blood picture. The lymphatic reaction is characterized by much the same picture, with the exception of a less pronounced leukocytosis or even a normal leukocyte count with a very high percentage of lymphocytes. The differential diagnosis is really made in the red blood picture as the person with merely a lymphatic reaction does not show the thrombopenia; in other words, does not show a true injury of the erythropoietic system. In a careful study of the family history and family types in twenty families, the author found that wherever a lymphatic leukemia is noted, members of the family show a much higher percentage of lymphatic reactions than other families do. The author concludes that there is a marked familial and constitutional factor in lymphatic leukemia.

GERSTLEY, Chicago.

THE PATHOLOGY AND CLASSIFICATION OF THE GENERALIZED "LIPOIDOSEN" (DISTURBANCES OF LIPOID METABOLISM) FROM THE CHEMICAL AND PHYSICOCHEMICAL POINT OF VIEW. DEGENERATION OF LIPOID CELLS AND ACCUMULATION OF LIPOID IN THE CELLS. EMIL EPSTEIN, Virchows Arch. f. path. Anat. **287**:152, 1931.

On the basis of his own chemical and physicochemical studies and those of other authors, Epstein attempts to differentiate between four definite disturbances of lipoid metabolism: 1. Niemann-Pick's disease, which is characterized by the presence of lecithin in the cells. It is called phosphatide cell lipoidosis. 2. Gaucher's disease, distinguished by the predominance of the cerebroside kerasin. It is called cerebroside cellular lipoidosis. 3. Christian's disease, in which the cells predominantly contain cholesterol and its esters. It is called cholesterol cell lipoidosis. 4. Xanthomatosis or xanthelasma, in which the cells show an accumulation of cholesterol. It is called cholesterol cell lipoidosis. Furthermore, a sharp line is drawn between Niemann-Pick's disease and the other conditions. In Niemann-Pick's disease a passive destruction of the cells takes place, while in the three other conditions mentioned, the cells seem to play an active part in the accumulation of the lipoids. Accordingly, Niemann-Pick's disease is spoken of as "Phosphatid Zellverfettungslipoidose" (a degenerative condition), whereas the other conditions are called "Speicherungslipoidosen" (storage lipoidosis).

SCHOENTHAL, New York.

THE PATHOLOGY OF PYLORIC HYPERTROPHY. H. BEUMER and R. HÜCKEL, Ztschr. f. Kinderh. **52**:136, 1931.

Beumer and Hückel disprove the notion that the greater incidence of pyloric hypertrophy in males is due to a hormone that, in the female, acts on muscles of the uterus. Measurements of fixed specimens of the pyloric rings of new-born babies did not reveal any definite relation between sex and the thickness of the pyloric musculature.

SHELLING, Baltimore.

CLINICAL OBSERVATIONS IN A CASE OF CYSTIC KIDNEY IN A TEN YEAR OLD GIRL. T. HALBERSTMA, Ztschr. f. Kinderh. **52**:145, 1931.

Halberstma describes a case of cystic kidney in a girl of 10 years. The diagnosis was corroborated by pylography. In spite of a large palpable tumor in the flank, hematuria and hypertension, the patient's physical condition was fairly good. Her father had had symptoms of bilateral cystic kidneys for the past sixteen years. His physical condition was only fair, and the blood nitrogen retention was quite high. The cases are presented because of the rarity of cystic kidney in older children and because of the familial or hereditary factors in the cases described.

SHELLING, Baltimore.

DIABETES INSIPIDUS WITH FAMILIAL TENDENCY. C. SUGIMOTO, J. Pediat. (TOKYO), Sept. 20, 1931, no. 376, p. 1235.

A case of diabetes insipidus occurred in a boy, 4 years and 9 months of age, with typical symptoms of polydipsia and polyuria. The mother suffered from the same ailment, and her symptoms became aggravated during pregnancy. Two other children of the same mother also showed similar symptoms. The mother stated that all these children were hydrophilic and fond of taking baths; they would eagerly drink the tub water, there being no hydrant in the bathroom. It is interesting to note that, as the result of a conference of the relatives on the husband's side, the mother was ordered to obtain a divorce because of this hereditary disease.

KATO, Chicago.

METROPATHIA HEMORRHAGICA JUVENILIS. NILS GYLLENSVÄRD, Acta obst. et gynec. Scandinav. **11**:423, 1931.

The author stresses the importance of distinguishing between acyclic and cyclic hemorrhages. He has selected a group of cases corresponding to the condition described by Schroeder as metropathia hemorrhagica juvenilis. He studied the onset, course and prognosis, and found that the mean age of the menarche averaged lower than in normal women. The first pathologic hemorrhage began with the menarche in only a small number of cases, and in most there was a period of several years of normal menstruation between the menarche and the appearance of the disease. Because of the significance of the hypophysis for ovarian function, and because both are intimately associated with the thyroid gland, the author studied the relationship of the latter to these uterine hemorrhages. He concluded that while there may be some disturbance of thyroid function in a few cases, one is not justified in assuming that it is responsible in all cases. The author studied his cases for from one to nine years and found good results from a variety of treatments for a few months. Relapses generally recurred during the second half year after treatment.

ADAIR, Chicago.

HEMATURIA IN CHILDREN. J. C. SCHIPPERS, Maandschr. v. kindergeneesk. **1**:10 (Oct.) 1931.

The author first describes a patient suffering from hemolytic jaundice and at the same time from paroxysmal hemoglobinuria. He then gives a short description of the several circumstances under which hemorrhages of the kidney may occur in childhood, illustrated by several observed cases.

VAN CREVELD, Amsterdam, Holland.

THE RÔLE OF COPPER IN ANEMIA IN CHILDHOOD. E. GORTER, F. GRENDEL and W. A. M. WEYERS, Maandschr. v. kindergeneesk. **1**:70 (Nov.) 1931.

In relation to the recent investigations of Hart, Steenbock, Elvehjem and others as to the significance of copper for the formation of hemoglobin, the authors

examined: (*a*) milk of different origin, (*b*) several iron preparations and (*c*) the blood of children with anemia for their copper content. The microtechnic used for the determination of copper is described (see also Grendel: *Pharmac. Weekblad,* 1930). The normal amount of copper in the total blood was found to be from 1 to 2 mg. per liter, the mean value being 1.4 mg. In the blood of new-born babies only from 0.7 to 1.4 mg. per liter (mean, 1 mg.) was found. Pregnancy and infectious diseases may increase the copper content of the blood. In seventeen determinations made in children with anemia the copper content of the blood was never lower than normal; the mean value was 2.1 mg.

VAN CREVELD, Amsterdam, Holland.

A CASE OF DERMOID CYST IN THE THORAX OF A CHILD. A. JONKER, Maandschr. v. kindergeneesk. **1**:87 (Nov.) 1931.

A case of purulent dermoid cyst arising either from the anterior mediastinum or from the right lung is described in a girl of 4 years. From the beginning the tumor was very large, which would be in favor of the theory that it was congenital.

VAN CREVELD, Amsterdam, Holland.

ROENTGEN RECOGNITION OF CONGENITAL HYPERTROPHIC PYLORIC STENOSIS. T. MEUWISSEN and J. P. SLOOF, Maandschr. v. kindergeneesk. **1**:107 (Dec.) 1931.

The authors are of the opinion that in all cases of vomiting in babies roentgen examination is necessary for an exact diagnosis. They use a special technic to make the pyloric canal visible. This is thought to be of primary importance. The retention phenomenon is next in importance. In hypertrophic pyloric stenosis the roentgen examination shows a long narrow pyloric canal. After operation, and sometimes also in patients cured without operation, the diameter of the canal gradually increases. Pyloric spasm is regarded as the cause of the clinical picture; the pyloric hypertrophy is probably the consequence of the spasm. With their technic of roentgen examination the authors also found that one cannot speak of a "normal" form or a "normal" location of the stomach.

VAN CREVELD, Amsterdam, Holland.

THE CAUSE OF ALBUMINURIA IN NEPHROSIS. L. J. DEL BAERE, Nederl. tijdschr. v. geneesk. **75**:3694 (July 11) 1931.

The author performed dialysis experiments with collodion sacks made permeable for proteins to a high degree by mixing the original solution of collodion with water. With such sacks he found that in nephrosis the most easily diffusible proteins have disappeared from the blood. The cause of the albuminuria is therefore due to an increased permeability of the kidneys. It is the author's opinion that these changes in the protein content of the blood also cause in nephrosis the development of edema at a much lower pressure than usual.

VAN CREVELD, Amsterdam, Holland.

MYXEDEMA, TRANSITORY EDEMA, CACHEXIA STRUMIPRIVA AND EPILEPSY. G. C. BOLTEN, Nederl. tijdschr. v. geneesk. **75**:4650 (Sept. 12) 1931.

In cases of myxedema and of transitory edema epileptic convulsions occur now and then, as the author illustrates with several examples. In animals epileptic and tetanic attacks appear always without exception after complete thyroparathyroidectomy; the same has been observed again and again in patients after complete strumectomy. From these facts the author concludes that the cause of genuine epilepsy must be sought in an insufficiency of the thyroid gland or in a pluriglandular insufficiency.

VAN CREVELD, Amsterdam, Holland.

Nervous Diseases

NEUROSOMATIC DETERIORATION IN EPILEPSY: A CLINICOPATHOLOGIC CONTRIBUTION TO THE CONCEPT, WITH A REPORT OF TWO CASES. MORGAN B. HODSKINS and PAUL I. YAKOVLEV, Arch. Neurol. & Psychiat. **27**:113 (Jan.) 1932.

Pathologic studies of two cases are reported. The first case was that of an apparently normal boy in whom encephalitis developed at 3½ years of age followed by spasticity on one side, which cleared up. A month later convulsions developed with mental deterioration, and he was committed to an institution as feeble-minded at 6 years of age. The deterioration continued with generalized muscular rigidity, pseudobulbar symptoms, increased frequency of epileptic attacks and death at 12 years. The second case was that of a man in whom epilepsy developed with cerebral arteriosclerosis and cardiorenal disease.

Pathologically, in both cases, there was evidence of: (1) a primary vascular lesion which, in the first case, was an acute inflammatory lesion (meningoencephalitis), and in the second case, a chronic noninflammatory lesion (cerebral arteriosclerosis); (2) a resulting or secondary chronic degenerative and atrophic lesion affecting primarily the frontal cortex and basal ganglions and characterized by (*a*) dropping out of nerve cells, (*b*) diffuse proliferation of glial cells and (*c*) chronic atrophy and degeneration of nerve cells. These pathologic changes are regarded as the pathology of neurosomatic degeneration. It was suggested that the degeneration of the complex frontopallido-mesencephalic system of the brain clinically is expressed by a progressive psychomotor syndrome consisting of a chronic convulsive state, dementia and rigidity, eventually leading to a cerebral flexion paraplegia. The acute and severe circulatory changes in the brain are constant phenomena. These changes in the medulla are terminal, and may explain the death by acute bulbar paralysis that results from status epilepticus.

Chronic changes in the visceral organs, especially the liver, which were present may be considered as the visceral component of the pathology of neurosomatic deterioration.

BEVERLY, Chicago.

HYDROCEPHALUS: REPORT OF A CASE IN AN INFANT WITH VESTIGES OF A CHOROID PLEXUS IN THE FOURTH VENTRICLE ONLY. GEORGE B. HASSIN, Arch. Neurol. & Psychiat. **27**:406 (Feb.) 1932.

The author reports a case of hydrocephalus with spina bifida and resulting purulent Staphylococcus albus meningitis. There was marked hydrocephalus due to obstruction of the third ventricle. This hydrocephalus developed in the almost total absence of the choroid plexus. The case is given as additional proof that the spinal fluid does not originate from the choroid plexus.

BEVERLY, Chicago.

THE ETIOLOGY OF BEHAVIOR DISORDERS AND PERSONALITY PROBLEMS. KENNETH APPEL, M. Clin. North America **15**:353 (Sept.) 1931.

Behavior disorders in childhood do not just happen, but are usually meaningful. In the background is an attempt on the part of the child to win something that his personality craves. If this is found, it will almost always be possible to satisfy it by some socially approved activity. The fundamental needs of children, the lack of which is behind most of the behavior disorders of children and adults as well, may be summarized as follows: health; security and love; independence appropriate to age; activity that is interesting and instructive, i. e., achieving something for the individual, and the recognition and friendship of contemporaries. Of first importance in meeting these difficulties and delinquencies is the adoption of an inquiring and optimistic outlook. The first thought should not be discipline, training and punishment, but curiosity, understanding and sympathy. One should try to see children objectively, to give them a background of security and wise encouragement in their attempt to win independence, to capitalize assets rather than liabilities and to deemotionalize tense situations.

SMITH, Ogden, Utah.

THE BLOOD GROUPING OF MONGOLIAN IMBECILES. L. S. PENROSE, Lancet **1**:394 (Feb. 20) 1932.

The distribution of the four blood groups was studied in 166 mongolian imbeciles. The results do not support the hypothesis that this class of imbeciles has any relationship to the Mongolian race.

LANGMANN, New York.

ENCEPHALITIS LETHARGICA. W. G. WYLLIE, Proc. Roy. Soc. Med. **24**:1184 (July) 1931.

This case was reported in a boy of 8 years who gave no history of an acute attack of encephalitis or of influenza. At the age of 5 years his right arm and leg began gradually to become weak, and he tended to fall over toward the right. The power of balance was lost. There were generalized extrapyramidal rigidity and a coarse tremor of the hands on exertion. The face was masklike, and the knee jerks were feeble. The child had become obese, and some hirsuties of the pubis had developed.

WILLIAMSON, New Orleans.

RADIOTHERAPY IN THE TREATMENT OF INFANTILE PARALYSIS (DISEASE OF HEINE-MEDIN). EMILIO BIDOLI, Clin. pediat. **13**:950 (Dec.) 1931.

From observations made in fifty cases of infantile paralysis during an epidemic, followed from the beginning of the disease until completion of the treatment, the author believes that the system of treatment advocated by Bordier in conjunction with diathermy and electrotherapy is the method of treatment productive of more constant and better results than are obtained by any other method. It is necessary, however, that this treatment be started early in the disease and carried on intensively. When evidence is present that irreparable damage has resulted to the cells of the anterior gray horns of the spinal cord, it is usually impossible to obtain favorable results from radiotherapy.

SIGNORELLI, New Orleans.

PNEUMOCOCCIC MENINGITIS WITH CLEAR CEREBROSPINAL FLUID. ROGELIO CHARLONE, Arch. de pediat. d. Uruguay **2**:291 (June) 1931.

This condition occurred in a boy 2 years of age who presented a general appearance of acute purulent meningitis. Although the spinal fluid was entirely clear, it contained a considerable number of lymphocytes and showed no microbes. At autopsy, yellow-green pus was found over the two cerebral hemispheres and extended toward the base. There was a bilateral bronchopneumonia. Bacterial examination revealed the presence of pneumococci.

SCHLUTZ, Chicago.

FAMILIAL SPASTIC PARAPLEGIA. LUIS MORQUIO, Arch. de pediat. d. Uruguay **2**:383 (Aug.) 1931.

The author has observed this condition in two pairs of brothers, 5 and 10 years of age, and 3½ and 5 years of age. In one of the cases there was asphyxia at birth with a possibility of cerebral hemorrhage. In the other cases the births were apparently normal. The antecedents were free from any neurologic disabilities, although the father of the last two patients was considerably retarded in walking.

SCHLUTZ, Chicago.

MENINGITIS DUE TO PFEIFFER'S BACILLUS IN AN INFANT OF NINE MONTHS. MARIA LUISA SALDUN, Arch. de pediat. d. Uruguay **2**:440 (Sept.) 1931.

The case reported occurred in an infant of 9 months, who presented all the symptoms of acute meningitis with purulent cerebrospinal fluid. The cerebrospinal fluid had a high cellular content and showed Pfeiffer's bacillus in large numbers.

SCHLUTZ, Chicago.

THE TOXICITY OF THALLIUM IN INFANTS. H. KLEINMANN, Arch. f. Dermat. u. Syph. **164**:181, 1931.

A 9 months old child was given 8 mg. of thallium acetate per kilogram. Toxic nervous symptoms developed from which recovery occurred after three months. The author considers thallium to be more toxic for infants than for older children.

MONASH, New York. [ARCH. DERMAT. & SYPH.]

TWO CASES OF MENINGITIS IN INFANTS DUE TO INFECTION WITH THE INFLUENZA BACILLUS. KARL RUPILIUS, Arch. f. Kinderh. **94**:307 (Oct. 23) 1931.

In both cases the meningitis was secondary to an infection of the lungs. Death occurred three days after the onset of the meningitis in one case, and five days after it in the other. The spinal fluid contained many cells of the polymorphonuclear type, and the influenza bacillus was obtained from cultures.

LESLIE, Evanston, Ill.

A DEVELOPMENTAL DEFECT AND A MIXED TUMOR OF THE CENTRAL NERVOUS SYSTEM. BEATRICE CHASAN, Schweiz. Arch. f. Neurol. u. Psychiat. **27**: 64, 1931.

Chasan presents the results of a careful anatomic study of the brain of a monstrosity that lived for two days after birth. The head was deformed; the left eye and left nostril were absent, the left cheek and region of the left side of the forehead being covered by a subcutaneous, tumor-like mass. The penis was of a rudimentary type. Aside from a definite microgyria, the right side of the cerebrum appeared to be normal. The left side of the cerebrum consisted of a collection of nodular masses, some of which were lobulated. It was attached at its base to the right hemisphere, but the corpus callosum was lacking. The surface of one of the nodules on the upper and outer part of the left hemisphere resembled that of a normal cerebellum. The left cerebellar hemisphere was smaller than the right; the left pyramid was altogether lacking.

Microscopic examination of the brain stem revealed a reasonably good state of preservation of the centers essential to life. A hyperplasia of the left dentate nucleus and brachium conjunctivum appeared to compensate for the relative hypoplasia of the left neocerebellar structures. The left abducens nerve was lacking; the left third nerve was poorly myelinated and seemed to disappear in a mass of undifferentiated tissue occupying the middle fossa of the skull.

The roof of the dilated third ventricle was open and the left lateral ventricle was apparently replaced by a series of intercommunicating cystlike spaces containing a rudimentary choroid plexus. One of these spaces was surrounded by a mass of tissue containing bone, cartilage and bits of choroid plexus, as well as undifferentiated tissue. A heterotopic midbrain anlage, containing a central canal and a structure resembling the red nucleus, was also found in the substance of the left hemisphere. The cerebellar anlage on the surface of this hemisphere was of typical cerebellar structure, including a rudimentary dentate nucleus. The surface tissue anterior to the cerebellar anlage had the structure of embryonic cortex. There was an arrhinencephaly on the left, and the central portion of the visual system was poorly developed on that side.

The author believes that the developmental defects arose from "a primary, endogenous injury of the germ plasm anlage" (*Keimanlage*) rather than from intra-uterine disease, this belief being supported by the fact that, although the father was alcoholic, the mother had previously given birth to a monstrosity. The mass of tissue in the substance of the left hemisphere was classified as a mixed tumor rather than as a teratoma.

DANIELS, Rochester, Minn. [ARCH. NEUROL. & PSYCHIAT.]

TUMORS OF THE BRAIN IN CHILDREN WITH THE CLINICAL PICTURE OF ACUTE ENCEPHALITIS. H. KNAUER, Jahrb. f. Kinderh. **133**:307 (Nov.) 1931.

The author presents the details of two cases of tumor of the brain. In each the test for encephalitis on the cornea of the rabbit gave negative results (Knaur and Jaensch: *Jahrb. f. Kinderh.* **130**:265, 1931). CLAUSEN, Rochester, N. Y.

THE STRIATE BLOOD SYNDROME IN A CASE OF CHOREA MINOR. H. SIMMEL, München. med. Wchnschr. **78**:660 (April 17) 1931.

The oxidase stain for the ferment associated with the granules of myeloid cells has been used in the differentiation of lymphoid from myeloid cells in various blood dyscrasias. Another ferment associated with the myeloid granules can be detected by the peroxidase stain of Sato and Sekiya. Normally both ferments are present. Several Japanese investigators have found that in epidemic encephalitis the peroxidase reaction becomes negative but the oxidase reaction persists—the so-called striate blood picture. Simmel presents a case of chorea minor (with report of autopsy) in which he found the striate blood picture. The patient, aged 8 years, had a history of polyarthritis, polyneuritis, endocarditis and recurrent chorea. During an attack of chorea the peroxidase stain was negative, but became positive during convalescence. The child died the day after an accident, and autopsy was performed. There was extensive degeneration of the ganglion cells in the striatum and nucleus ruber with evidence of neuronophagia. There was diminution in the cells of the dentate nucleus.

BRAHDY, Mount Vernon, N. Y.

THE MOTOR DEVELOPMENT OF CHILDREN SUFFERING FROM STAMMERING: THE NEUROPSYCHIATRIC PROBLEMS OF ADOLESCENCE. COLLECTED PAPERS. Ukrainian State Neuropsychiatric Institute **16**:81, 1931.

Fifty school children who stammered were studied from the point of view of intelligence and motor endowment by the methods of Ozeretzky and Quint. The children were both male and female, and varied in nationality, race and age. The following conclusions were reached: (1) The intellectual development is usually above normal; (2) the motor development is considerably ahead of the chronologic age; (3) the inadequate motor development found in some cases is usually associated with mental deficiency; (4) stammerers who are well developed intellectually are also well developed from the motor point of view; (5) the mimicry and facial expression are affected by stammering.

KASANIN, Howard, R. I. [ARCH. NEUROL. & PSYCHIAT.]

JUDGMENT OF THE DEEP REFLEXES. G. BERGMARK, Acta med. Scandinav. **76**: 5, 1931.

Two cases are reported (one confirmed by autopsy) of amyotrophic lateral sclerosis in which the knee jerk was diminished to a stimulus of ordinary force but in which the same diminished response was obtained with a stimulus too slight to be effective in producing any response in normal persons. On the evidence of diminished knee jerk an erroneous diagnosis of alcoholic neuritis had been made previously.

KAJDI, Baltimore.

THE EFFECTS OF VARIOUS IODIZED OILS ON THE MENINGES. ADOLF F. LINDBLOM, Acta med. Scandinav. **76**:395, 1931.

The author studied the biologic effects of iodized oils on the meninges in rabbits. The iodized vegetable oils do not produce irritation except when impurities, such as free fatty acids or iodic fatty acids and hydrogen iodide, are present. The impurities are absorbed rapidly and the iodized oil itself very

slowly, sometimes giving rise to "fatty granulomas." The iodized animal oils (cod liver oil) produce severe meningitis, even without impurities, because they are emulsified in the cerebrospinal fluid and a rapid splitting takes place, the products of which are very irritative; these oils are therefore not suitable contrast mediums for use in roentgen diagnosis.

KAJDI, Baltimore.

Diseases of the Eye

HEMANGIOMA OF THE CILIARY BODY. R. K. DAILY, Am. J. Ophth. **14**:653 (July) 1931.

An infant of 5 months suffered severe pain, apparently from an inflamed right eye. The mother stated that the child had had recurrent hemorrhages into the anterior chamber. The tuberculin and Wassermann reactions were negative. When first seen, the tension was high, and the anterior chamber was filled with blood. When this blood was absorbed, a narrow, dark brown growth could be seen in the angle of the anterior chamber, nasally. The eye was enucleated, and a dense neoplasm was found in the ciliary body, 7 mm. long, the width of the ciliary body, and 1.5 mm. thick. It produced an iridodialysis, and a portion projected into the anterior chamber at the filtration angle. Microscopic examination showed numerous capillary vessels between which were cords of rather large cells with vesicular nuclei. The diagnosis was capillary hemangioma of the ciliary body.

REESE, Philadelphia. [ARCH. OPHTH.]

STRABISMUS IN CHILDREN. DONALD L. LYLE, Arch. Pediat. **48**:619 (Oct.) 1931.

Observations in eighty cases of strabismus from the Children's Hospital of Cincinnati and the author's private practice are reported. It was found that four fifths of the blindness or useless vision in children studied was due, not to injury or disease of the eye, but to strabismus. The author states that the majority of patients can be greatly benefited if given early and proper care. He describes the various types known and the theoretical causes, methods of examination and therapeutic procedures. He makes the plea that such cases be referred to the oculist early in life, when good results can be expected.

WADDELL, University, Va.

MYELOMA OF THE ORBIT. Fourth Ann. Rep. Giza Mem. Ophth. Lab., 1929, p. 42.

The patient was a girl, aged 8 years. Proptosis of the left eye had begun two months previously and was extreme. A tumor of firm consistence could be felt in the roof of the orbit. Later the cornea sloughed. The orbit was exenterated. Three months later it was filled with a recurrent growth, and there was a large swelling of bony consistence in the region of the maxillary antrum. There was no adenopathy. On the ground of the morphology of the cells, the tumor was probably a myeloma. It was not of the plasma cell type, but myeloblasts, myelocytes and erythroblasts, all embryonal, were present. There was some doubt that the tumor was primary.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

HEREDITARY ASPECTS OF LEBER'S OPTIC ATROPHY. W. RITCHIE RUSSELL, Lancet **2**:1018 (Nov. 7) 1931.

Four cases of Leber's optic atrophy are reported in an Orcadian family, all in the same generation. The parents were second cousins. No history of the disease in the preceding generation could be obtained. The patients were all in the third stage of life when seen, one fixing the onset of failing vision at the age of 20. The author speculates on whether a second factor, not sex-linked, and

multiplied by the consanguinity, was concerned in the manifestation of the disease. The other possibility is that consanguinity had reduced the general vigor of the stock in some way, with the result that a dormant trait manifested itself again.

LANGMANN, New York.

UNILATERAL EXOPHTHALMOS. A. F. MACCALLAM, Proc. Roy. Soc. Med. **24**: 1182 (July) 1931.

A case of unilateral exophthalmos was reported in a boy of 8 years. In September, 1930, his left eye began to protrude and grew steadily more prominent. Suggested diagnoses were periosteal sarcoma of the orbit, angioma or mucocele of the frontal sinus. An operation performed in April, 1931, revealed a spongy diploic bone filling the whole of the frontal sinus and extending down to apparently healthy dura.

WILLIAMSON, New Orleans.

PRIMARY SARCOMA OF THE CARUNCLE AND SEMILUNAR FOLD. ALEXIADÈS, Arch. d'opht. **48**:341 (May) 1931.

The author points out that tumors of the caruncle and semilunar fold are infrequent. The majority of new growths in the caruncle are of epithelial origin. He refers to some of the cases that have been reported in the literature. The tumors arising from the semilunar fold are more often sarcoma. He reports the case of a 7 year old boy who presented a large reddish mass in the inner canthal region. This was completely removed surgically, and no recurrence was noted after more than a year's observation. Histologic examination showed it to be a round cell sarcoma. Anatomic and histologic study showed no evidence of the presence of either caruncular tissue or of the semilunar fold. The author suggests that the tumor probably arose from the semilunar fold and invaded and destroyed the caruncle.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.].

CONGENITAL CYST OF THE ORBIT OF ETHMOIDAL ORIGIN. P. VANCEA, Riv. oto-neuro-oftal. **8**:222 (May-June) 1931.

A congenital cyst of the orbit not associated with a developmental anomaly of the eyeball is very rare. The only similar case described by Panas in his treatise of 1894 was ascribed to a lacrimal origin. The author has a different point of view. His patient presented a normal eyeball and a cyst situated in the lower and inner angle of its orbit. The swelling appeared soon after birth and was associated with a homolateral congenital anomaly of refraction. Its congenital origin seems, therefore, beyond dispute. Vancea admits the possibility of a fetal and intra-orbital inclusion of ethmoid mucosa because ethmoid cells are already formed in a six months embryo and are developed at birth; their cell walls nearest the orbit are very thin, and the corresponding os planum is often dehiscent between its anterior and posterior two-thirds. In the latter condition the ethmoid cells have wide orbital openings and are separated from the orbital cavity by very thin periosteum. At operation the cyst pedicle was followed through to the medial orbital wall, i. e., to those ethmoid cells (agger nasi or preinfundibular cells) which almost surround the lacrimal fossa. Some have called them lacrimal cells because Stanculeanu (1902) showed that they open into the anterior superior portion of the unciform fossa. This makes it clear why an anterior ethmoiditis may produce pain here, made worse by pressure, and why all collections and new formations here tend to appear in the lower and inner angle of the orbit in proximity to the lacrimal sac. Moreover, no sebaceous glands exist in the mucosa lining the lacrimal passages. Such glands are present in the mucosa of the paranasal sinuses. Histologic examination of the cyst extirpated from the author's

patient showed the presence of sebaceous glands, thus confirming its ethmoidal origin. The cyst wall showed a diffuse lymphocytic infiltration and a marked hyaline degeneration at its periphery so characteristic of old congenital cysts and so rare in young persons. These degenerative changes in a young patient (22 years) had not yet become generalized through the entire cyst.

SYRACUSE, New York [ARCH. OPHTH.].

EARLY CATARACT IN A BOY AGED FOUR YEARS. R. R. GIL and A. G. FUEROL, Rev. de especialid. **7**:962 (Oct.) 1931.

The author presents a case of early cataract in a 4 year old boy. Photomicrographs of the condition are shown. The treatment was extraction in toto, which was successful.

SANFORD, Chicago.

CONGENITAL ANIRIDIA. R. R. GIL and A. L. RIVAS, Rev. de especialid. **7**:998 (Oct.) 1931.

The authors discuss congenital aniridia, or malformation of the anterior uveal tract, which is frequently bilateral and results in an apparent absence of the iris. Its characteristic appearance is an apparent absence of the pupil. Glaucoma is a frequent complication. Various methods of treatment have been advocated, but are unsatisfactory.

SANFORD, Chicago.

VARIOUS FORMS OF CONGENITAL CATARACT. TAWADO OGUCHI, Acta Jap. Ophth. Soc., May, 1931, p. 36.

The author has reported on the slit-lamp findings in various forms of congenital cataract. 1. Anterior axial embryonal cataract. This form was observed in about 22.6 per cent. 2. Anterior and posterior embryonal suture cataract. This form is not as frequent as the preceding, and differs from it by the fact that the suture itself is clouded. This opacity may affect the posterior as well as the anterior suture. Four cases of this cataract are described. 3. Dilacerated cataract. This has been described by Vogt as very unusual and involves the deeper layers of the adult nucleus and the axial zone. The author has been able to find three cases in which the cataract consisted of flat, irregular opacities with axes consisting of white dots and lines. 4. Coralliform cataract. This is a peculiar axial cataract described by several English observers, which appears in various layers of the lens. The "Spiess" cataract, observed by Vogt, and later by Gifford, probably belongs to this variety. The author has found a family in which this cataract was observed in three generations. 5. Central powdered cataract. This condition, first described by Vogt, has been observed by the author in two cases. The outline of the cataract is well defined. The dots are very fine and frequently run into one another. 6. Incomplete zonular cataract. 7. Two particular forms of central cataract.

KNAPP, New York. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

ROENTGENOLOGIC STUDY OF MASTOID IN INFANTS. CHARLES L. MARTIN, Am. J. Roentgenol. **22**:431 (Nov.) 1929.

A review of the literature reveals some diversity of opinion as to the time of pneumatization of the mastoid in infancy. After 6 months of age a cavity having the shape of the mastoid can be demonstrated below the tegmen tympani and behind the external auditory meatus in good roentgenograms. The cavity varies markedly in size and may measure as much as ¾ inch (1.9 cm.) in diameter and show definite cell structure at 9 months. Diploetic mastoids are probably

such from the start, whereas cellular mastoids begin as large single cavities which slowly increase in size and usually begin to show cellular structure at from 9 to 16 months. The presence of pathologic conditions of the mastoid can usually be detected in good roentgenograms after the age of 6 months, though double infection often makes interpretation difficult. A bibliography is appended.

STULIK, Chicago.

A NEW AND EFFECTIVE NON-SURGICAL METHOD FOR THE TREATMENT OF CHRONIC SUPPURATION OF THE MIDDLE EAR. CHARLES HYMES, Minnesota Med. **14**:1054 (Dec.) 1931.

The author recommends insufflation into the middle ear, by means of low pressure, of a mixture of potassium iodide crystals, 1 part, and powdered boric acid, 3 parts. The treatment is continued from two to three times weekly, seldom longer than three weeks. Marked success is claimed even when a chronic discharge persists after a radical mastoid operation. Hymes reports in some detail a series of twenty cases.

HUENEKENS, Minneapolis.

OTOGENOUS GENERALIZED INFECTION IN NURSLING AGE. I. HOFER, Monatschr. f. Ohrenh. **66**:462 (April) 1932.

Following an introductory discussion of the differentiation of various types of generalized infection, Hofer reports a case of otogenous sinus thrombosis with toxemia, in a nursling of 10½ months, whom he was able to cure by surgical exclusion of the infectious focus. The infant was hospitalized because of eczema, influenza, rhinitis, bronchitis and bilateral otitis media. About three weeks later, after a slight amelioration of some of the disturbances, the otitis on the right side became acute, giving rise to mastoiditis. Neither antrotomy nor exposure and resection of the sigmoid sinus performed two weeks later were able to end the marked intermittent fever, and it was only after ligation of the right jugular vein and exclusion of the septic focus, constituted by the thrombus in the sigmoid sinus, from the circulation that the temperature dropped and a marked improvement in the general condition took place. The author designates this case of septic generalized infection as an instance of toxemia because no bacteria could be demonstrated in several cultural examinations of the blood, and the condition, therefore, could not properly be called bacteremia. He does not call it pyemia, although the intermittent fever curve was characteristic of pyemia, because no metastases occurred. The author says that otologists must keep in mind that the occurrence of otogenous generalized infection, whether pyemic or of some other form, is not as rare in nurslings as many pediatricians believe. Usually these cases have a rapid fatal termination because the nurslings cannot resist a septic process of long duration, especially when the location of the septic focus, as in otogenous cases, is not diagnosed and not surgically excluded.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

SPECIAL CLASSES FOR DEFECTS IN SPEECH. HANS DIRR, Ztschr. f. Kinderforsch. **39**:134 (Dec. 15) 1931.

The author advises the use of the phonograph in correcting defects in speech. He has also used the following method to interest these children, many of whom are mentally deficient, in the instruction: One child is sent to buy a bag of candy. The children are then taught a few simple phrases and given a piece of the candy if their request is properly articulated.

REICHLE, Cleveland.

Miscellaneous

OPEN SAFETY PIN IN THE STOMACH OF AN INFANT. H. J. HARA, California & West. Med. **37**:45 (July) 1932.

An infant, aged 2 months, was observed seven hours after the swallowing of an open safety pin. A roentgenogram taken as an emergency measure revealed the pin in the stomach. At the time of observation the child had a temperature of 102 F. and an elevation of leukocytes, explained, doubtless, by the findings of an acute coryza and beginning bronchopneumonia. Fluoroscopic examination revealed the pin lying freely movable in the fundus of the stomach, the spring portion toward the cardia. A duplicate pin, furnished by the mother, proved helpful in the study of the case. The following day roentgenographic studies revealed the pin in the small intestine and the following day, forty-three hours after its being swallowed, the pin was passed per rectum. It measured 3 cm. in length.

In the absence of organic pyloric stenosis, a majority of foreign objects that reach the stomach unassisted can be passed per rectum. In such cases, watchful waiting, with daily roentgenographic studies and without changes of diet or the administration of cathartics is recommended rather than hasty surgical intervention.

MARSHALL, San Francisco.

THE MANAGEMENT OF POSTURE IN CHILDREN. REGINALD H. WIGGINS, Canad. M. A. J. **27**:47 (July) 1932.

The author emphasizes the importance of proper posture in the growing child. He divides the management into two measures, preventive and active correction. Details as to exercises and special measures of correction are given.

The author believes that incorrect posture ranks with nervousness, fatigue and malnutrition and with these forms the quartet of conditions chiefly responsible for the present lack of progress in the physical and mental development, wellbeing and efficiency of the child.

MOORE, Omaha.

NEW PHASES IN PEDIATRIC MEDICINE. CLIFFORD G. GRULEE, Illinois M. J. **62**:130 (Aug.) 1932.

The medical schools in this country are not fulfilling their duty to the public in respect to the education of doctors who practice among children. The medical schools must find a way out or else not only on the medical schools but on the medical profession as well will fall the censure of the community. General hospitals are short on pediatric facilities. This is serious because the children who go to these hospitals do not have the intelligent supervision necessary to protect them from conditions in hospitals that are peculiarly disturbing to the young patient, and because the nurses trained in these hospitals do not receive the training that is essential to the intelligent care of children. The public needs to be aroused from its lethargy toward available preventive and immunizing measures. The teaching of health problems in schools is wofully inadequate, and much of it is wrong. The basic problem is medical education. Public health officials and members of the medical profession must get together on a common ground. Much can be accomplished if they work together, very little if they work separately. Pediatricians are ready and willing to proceed along sane lines for the betterment of children, whether it concerns their minds or bodies, but this procedure must be sure, and it must mean a cooperation of all forces in this work.

ORVILLE BARBOUR, Peoria, Ill.

KEROSENE POISONING IN CHILDREN. J. H. PRICE, J. A. M. A. **99**:214 (July 16) 1932.

There is no constant picture of kerosene poisoning. The most common picture is irritation of the alimentary tract, with burning in the mouth, throat and

stomach, colicky pains in the abdomen, vomiting, thirst and painful micturition. The more serious symptoms are drowsiness, cyanosis, shallow respiration, feeble pulse and coma. A bright cherry red color of the lips is sometimes found, and the analysis of the blood by spectrum shows methemoglobin. Treatment is unsatisfactory, consisting of gastric lavage and symptomatic treatment. There is no known antidote. The author reports four cases, in which one of the patients died.

BONAR, Salt Lake City.

THE BIOLOGIC ACTION OF ULTRA HIGH FREQUENCY CURRENTS. W. T. SZYMANOWSKI and R. A. HICKS, J. Infect. Dis. **50**:1 (Jan.) 1932.

Temperature in itself is not the only physical destructive agent of toxin, since ultra high frequency currents may accomplish this same result without any change in temperature. This article is comprehensive and contains good references to all the fundamental work along this line.

TOOMEY, Cleveland.

RECORDED AND RESIDENT DEATH RATES IN NEW YORK STATE. J. V. DEPORTE, New York State J. Med. **32**:257 (March 1) 1932.

In 1915 the infant mortality in New York was ninety-nine per thousand live births, and infant deaths represented 16.4 per cent of the mortality at all ages. In 1930 the death rate had dropped 41 per cent to fifty-eight per thousand, and represented but 8.6 per cent of the total mortality. The greatest improvements have been in the reduced deaths from gastro-intestinal and respiratory diseases.

An analysis of the relationship between the resident and recorded rates showed that the element of residence has but slight numerical effect on the recorded mortality rates throughout New York.

AIKMAN, Rochester, N. Y.

BIRTH, GENERAL MORTALITY AND INFANT MORTALITY STATISTICS IN THE BIRTH REGISTRATION AREA 1930. Pub. Health Rep. **47**:1647 (Aug. 5) 1932.

During 1930 the birth rate was 18.9 per thousand, and the death rate 11.3. New Mexico had the highest birth rate, 28.5, and Oregon the lowest, 14.1. The infant mortality rate was 64.6 (67.6 in 1929), New Mexico having the highest, 145.4, and Oregon the lowest, 50. This rate for the white race was 59.6, and for the colored race 102.4.

SANFORD, Chicago.

HYPERPYREXIA, A NEW FIELD FOR PHYSICAL THERAPEUTICS. CLARENCE A. NEYMANN, Brit. J. Phys. Med. **6**:141 (Oct.) 1931.

A method of producing hyperpyrexia by diathermy was described. A temperature of 104.5 F. could be produced in from one and a half to two hours. It was reported that some patients required only a slight application of the current to maintain temperature between 103.5 and 105.5 F. for five, six or even eight hours. Other patients required two, three or even more applications to maintain this range of temperature. A pyrometer for making a continual record of rectal temperatures was also described. It was claimed that with a correct technic this method of producing fever could be controlled with accuracy. The dangers were said to be extremely slight, and it was claimed that they could be entirely overcome by proper care and attention.

HARTMAN, Cleveland.

THE MEAN TEMPERATURE OF HEALTHY GIRLS. J. H. P. PATON, Brit. M. J. **2**:142 (July 23) 1932.

An investigation was made on a large number of girls from 14 to 17 years of age, and it was found that the variation in temperature during the day was considerable. The author believes that at this age the normal temperature is

97.4 F. rather than 98.4 F. In fact, he found that it was rare for the mean temperature to approximate 98.4 F., and he states that when the temperature of the mouth is 98.4 F. it really means some degree of fever.

ROYSTER, University, Va.

INTELLIGENCE AND DISEASE. SHEPHERD DAWSON, Medical Research Council, Special Report Series, no. 162, London, His Majesty's Stationery Office, 1931.

Binet intelligence tests were applied to 1,077 children in the Sick Children's Hospital, Glasgow. Those suffering from rheumatism, pneumonia, nephritis and other ailments, not of the brain, showed no change in intelligence, nor did those suffering from disease of the spinal cord. Those, however, in whom there was disease of the ductless glands and brain showed an appreciable departure from the normal in intelligence. Interesting exceptions were found in some cases of spastic diplegia and localized cerebral tumors; that is, there was no decrease in intelligence. Patients with chorea showed no change. Most cases of postencephalitis lethargica showed mental deterioration. Epileptic patients were of lower intelligence than their brothers and sisters. With acute illness there was a slight improvement in mental efficiency, while chronic illness had no effect. Children slightly taller than the average had a higher intelligence, and those of higher intelligence had, on the whole, begun to talk and walk at an earlier age than the others.

SANFORD, Chicago.

ALCOHOL AND INHERITANCE: AN EXPERIMENTAL STUDY. F. M. DURHAM and H. M. WOODS, Medical Research Council, Special Report Series, no. 168, 1932.

Guinea-pigs of both sexes were treated with alcohol for varying periods from one month to five years, and also four successive generations of guinea-pigs were so treated. There was no evidence to show that exposure to alcohol injured the germ cells, so that abnormal young were produced. Fertility and sex-ratio were unaffected by the treatment with alcohol. Deterioration in weight and increase in mortality of descendants occurred in the alcoholized animals only to a degree that could be accounted for by the inbreeding and by their increased age.

LEMASTER, Evanston, Ill.

A REVIEW OF THE PEDIATRIC LITERATURE OF RUSSIA DURING THE YEARS 1922 to 1930. D. D. LEBEDEFF, Arch. franç. de pédiat. **7**:496, 1931.

The author reviews the Russian literature on infant mortality, physiology, syphilis, tuberculosis, infections and contagious diseases, respiratory and gastrointestinal diseases, parasites and vascular and nervous disorders. Of especial interest is the infant mortality of 28.5 per cent in the cities and 29.5 per cent in the country districts in 1910, as compared with 17.3 per cent and 19 per cent, respectively, noted in 1926.

SANFORD, Chicago.

PEDIATRIC MEETINGS AT THE HAGUE, FLORENCE AND STRASBOURG. P. LEREBOULLET, Paris méd. **2**:363 (Nov. 7) 1931.

The International Congress of Preventive Pediatrics met at The Hague in September. The two most important subjects discussed were mortality of the new-born and scarlet fever. The Italian Congress of Pediatrics met at Florence in the latter part of September. Some of the more important matters discussed were maternal mortality, purulent pleurisy of infancy, encephalitis and directive dietetics. The French Pediatric Congress met at Strasbourg in October. Here alimentary fevers, cerebral tumors and avitaminoses were discussed.

SANFORD, Chicago.

THE MENTAL DEVELOPMENT OF TWINS. C. LOOFT, Acta pædiat. **12**:41, 1931.

Mental deficiency has for a long time been suspected of being common among twins. The author examined 703 backward school children. The percentage of twins was higher in this group than among normal children. The same applied to the combined populations of four districts in Norway in which a registry of imbeciles and idiots was kept. The incidence of twins was likewise higher among the siblings of mentally deficient children. Several groups of twins were given intelligence tests. The material is perhaps not sufficiently large for statistical evaluation, but the results indicated a higher frequency of mental inferiority. In general, the lower the weight at birth, the lower the intelligence quotient. A history of prolonged and difficult labor was frequently associated with mental retardation in one or both twins. There was a rather striking tendency for the I. Q. of identical twins to be the same in both individuals.

McINTOSH, New York.

ELECTROCARDIOGRAMS OF INFANTS DURING TREATMENT WITH COD LIVER OIL AND VIOSTEROL. I. JUNDELL and N. STENSTRÖM, Acta pædiat. **12**:113 (Sept. 30) 1931.

A study of the electric axis of the heart, by the method of Carter, Richter and Greene shows that during the first year of life there is an average swing in the angle α of from 130 to 45 degrees. The most rapid change occurs in the first four or five months. Shortly after birth the average auriculoventricular conduction time is 0.08 seconds; it increases in the first six months to about 0.09 seconds. The average Q-R-S time increases during the same interval from 0.05 to 0.06 seconds. The observed change in the auriculoventricular conduction time is not proportional to the growth in the size of the heart, and one must postulate an increased efficiency of the conducting system in the early period of growth. Infections of any sort cause prolongation of both the auriculoventricular interval and the Q-R-S complex. The authors believe that unavoidable infections in early life, by modifying conduction time in this way, prevent the heart from maintaining its initial conduction rates throughout life. A small series of infants was treated with cod liver oil, and electrocardiograms were taken at intervals of about two weeks. The authors report increases in both the auriculoventricular conduction time and the Q-R-S time of greater magnitude than would have been expected to result from unmodified growth. There were also irregular changes in the rotation of the electric axis and abnormalities of the T wave, particularly in lead III. A dose of 3 teaspoonfuls of cod liver oil a day brought out these changes in from one and a half to two months. Emulsified oil produced a more rapid and more marked effect. Viosterol, in a dosage corresponding to the antirachitic effect of 3 teaspoonfuls of cod liver oil, was similarily toxic. In one infant, irradiated egg yolk powder, 2 teaspoonfuls a day, produced identical changes. These investigations continued the animal experiments of Agduhr and Stenström previously abstracted in this journal (AM. J. DIS. CHILD. **39**:193 [Jan.] 1930; **40**:1101 [Nov.] 1930; **41**:415 [Feb.] 1931), on the influence of various antirachitic agents on the hearts of laboratory animals. Here again, the inadequacy of the control studies demands that one accept the authors' conclusions with reserve.

McINTOSH, New York.

REGISTRATION AND ELABORATION OF CLINICAL DATA. E. W. WALCH, Nederl. tijdschr. v. geneesk. **75**:4027 (Aug. 1) 1931.

The author discusses the newer statistical methods and their value in registration, elaboration and classification of clinical data. As an example he discusses the results of an investigation of infant mortality and the bodily development of 1 year old children in Batavia (the Dutch Indies).

VAN CREVELD, Amsterdam, Holland.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Annual Meeting, May 17, 1932

HENRY E. IRISH, M.D., *President, Presiding*

A CASE OF ACRODYNIA. DR. PHILIP L. ARIES.

A girl, 19 months old, is the only child of healthy young American parents. The mother has had no other pregnancies. The child was born at full term, and weighed 9½ pounds (4,309.13 Gm.) at birth. Until the present illness, the history was unimportant.

The child was entirely breast fed for eight months. Orange juice and cod liver oil were started at the age of 6 weeks and have been taken in sufficient amounts to the present time. Cereal was fed at 4 months; egg yolk at 5 months and soups and vegetables at 6 months. The child was weaned at 9 months, when she was given an adequate mixed diet.

Development took place normally. She sat up at 5 months, had her first tooth at 5 months and walked at 11 months. She uttered her first words at 1 year. The weight was 25 pounds (11.3 Kg.) at 1 year and 30 pounds (13.6 Kg.) at 16 months. She has sixteen teeth. She has had the advantages of excellent hygienic care.

The illness from which the child is now recovering began insidiously in February, 1932—eleven weeks ago. A change in disposition was first noticed. She became irritable and cried and whined a great deal, refused food and slept poorly. At the same time the hands and feet became red, cold and somewhat swollen. She often held her hands in her mouth and frequently bit them. After a week there was a tendency to avoid light, and in a bright place she buried her head in her clothing. She was not inclined to run about as usual. The temperature was normal, except on one occasion during the third week when it rose to 101 F. rectally. Some nasal discharge was noted at that time. During the fourth week an eruption on the trunk and upper extremities appeared in addition to the redness of the hands and feet. Perspiration became profuse. She ground her teeth and pulled out strands of hair. There was marked generalized itching, and the child refused to walk or even to stand. She preferred to be in a crouched position most of the time. Sleep was very poor. Food was constantly refused. The general state of misery was trying.

I saw the child on April 5, five weeks after the onset of this picture, and physical examination showed the following: The temperature was 100.8 F. rectally. The fontanels were closed. The tip of the nose and the chin were flushed. There was no nasal obstruction or discharge. The tonsils were moderately enlarged and somewhat cryptic, but not inflamed. The pharynx was slightly injected. The heart, lungs, abdomen and genitalia were normal.

The hands were pink,, cold and clammy. There was some swelling, but no pitting on pressure. The skin of the palms and around the finger-nails was desquamating, so that scarlet fever was at once brought to mind. There was no desquamation above the wrists. Tiny papules stood out about the finger tips. The redness of the hands merged with a patchy erythematous eruption on the forearms and arms which gradually faded as the shoulders were reached. The feet were cold and red, but no desquamation was noted at this time. There was practically no eruption on the legs or thighs.

A scarlatiniform eruption was present on the trunk and neck. The skin was rough and moist with perspiration. Excoriations and scratching were seen over

the lumbosacral areas and on the buttocks. A fine branny desquamation, which lasted only a few days, was seen on the back from the neck down to the waistline.

The reflexes were all normal.

The weight was 28½ pounds (12.9 Kg.), the child having lost only 1½ pounds (0.7 Kg.).

The laboratory findings were as follows: The urine was normal. Only a few epithelial cells were observed microscopically. The blood showed hemoglobin, 80 per cent, and red cell count, 4,100,000. The red cells were normal. The white blood cell count was 14,950. The differential count showed polymorphonuclear neutrophils 34 per cent, large and small lymphocytes 62 per cent, and eosinophils 4 per cent. The Mantoux test, with 0.05 cc. of a 1:250 dilution of older tuberculin, was negative. The Wassermann and Kahn reactions of the blood of the mother were negative. Throat culture showed Staphylococcus aureus. No Klebs-Loeffler bacilli or hemolytic streptococci were found.

A diagnosis of acrodynia of moderate severity was made.

The treatment consisted in feeding the child. This was difficult. Yeast, cod liver oil, viosterol and orange juice were added to the diet. Calamine lotion relieved the cutaneous condition. A course of treatments with ultraviolet rays was given.

On April 11, two weeks after desquamation of the hands and feet started, the soles began to desquamate. The general condition has gradually improved during the past three weeks. The temperature has always been about 100 F. rectally. At present the child sleeps well. She has a happier disposition than formerly but is not yet normal. The appetite is still poor. The photophobia disappeared after the fifth week. The nose and throat have been normal. The child walks about cautiously and does not tire as easily as when she started to exercise three weeks ago.

The hands are pink, appearing as if they had been soaking in cold water. Some fine desquamation can be seen on the palms. The feet are normal. A little peeling is noted between the toes.

Perspiration is still profuse. There is an erythematous flush over the skin of the trunk. Discrete papules are scattered over the same area. Some crusted excoriations are found on the back.

Congenital Atresia of the Duodenum. Dr. Milo K. Miller.

E., the first child of young healthy parents, was born at Epworth Hospital on Feb. 10, 1932. The weight at birth was 8 pounds and 10 ounces (3,912.24 Gm.). On the next day, following the giving of dextrose solution by mouth, he several times vomited projectilely a greenish-yellow fluid. A moderate distention of the upper part of the abdomen existed, and several times peristaltic waves were seen. No masses were felt. No stools except meconium were passed. A tentative diagnosis of obstruction of the duodenum was made.

Roentgen examination by Dr. Stanley Clark, on February 12, showed marked gastric spasm with obstruction, probably in the second portion of the duodenum.

The abdomen was explored by Dr. James Wilson on February 13, the third day of life. He found a markedly distended stomach, and the first portion of the duodenum with the intestine beyond the obstruction was perfectly flat. He released what appeared to be a peritoneal band at the site of obstruction and thought that some gas passed into the bowel below the obstruction. The abdomen was closed. The baby continued to vomit bile-stained material.

On February 15, the fifth day of life, a second operation was performed by Drs. Wilson and Clark. The stomach and duodenum were still distended. The duodenum was opened, and complete obstruction of the lower end was found. No opening could be found with a probe. A duodenojejunostomy was performed. The postoperative course was uneventful except for a superficial infection of the wound, which eventually healed completely.

Roentgen examination on February 18 showed the barium to be somewhat delayed in the stomach. The twenty hour plate showed barium scattered throughout the small intestine.

Vomiting practically ceased following the second operation. The baby has gained rapidly on breast feeding and at the present time, at a little over 3 months of age, weighs nearly 15 pounds (6,804 Gm.).

On May 5, when the child was nearly 3 months of age, another roentgen examination showed good motility of the stomach, all the barium having emptied in five hours.

As nearly as I can determine, less than a half dozen patients with congenital duodenal obstruction have survived. All authors agree that with more frequent early diagnosis more successes will be recorded. The characteristic symptom complex of vomiting of bile, upper abdominal distention and often peristaltic waves, rapid dehydration and constipation needs only to be borne in mind for these little patients to be given the benefit of early operative intervention.

Several types of congenital duodenal obstruction have been described: (*A*) extrinsic, caused by either (1) incomplete rotation, (2) peritoneal bands or (3) abnormal position of the anterior mesenteric artery; (*B*) intrinsic, which are (1) partial, caused by simple narrowing of the lumen, or (2) complete, caused by either (*a*) annular constriction, (*b*) complete membranous diaphragm or (*c*) atresia of a portion of the intestine, the upper segment ending in a culdesac and the lower segment a mere band.

A Case of Exstrophy of the Bladder: Malformation of the Lumbar Spine and Paralytic Ileus. Dr. King G. Woodward.

Exstrophy of the bladder occurs in about 1 of every 50,000 infants, with a sex incidence of 1 female to 8 males. The following case report is especially interesting because of the associated rare anomalies.

Z. was born at the Winnebago County Hospital on March 23, 1932, the fifth child of normal Italian parents. Labor was normal, and the child's condition was good at birth.

Examination revealed a small infant born prematurely at eight months, weighing 5 pounds and 8 ounces (2,494.76 Gm.) The head, thorax and extremities were normal, and no masses were felt in the upper part of the abdomen.

In the lower portion of the abdomen, involving the area immediately above the pubes and including the area of the external genitalia, there was a striking departure from the normal. In the region above the symphysis there was a yellowish-red mass about 5.5 cm. in diameter, extending 3 cm. above the surrounding abdominal wall, which had the appearance of mucous membrane. This was surrounded by normal skin at the base. Near the lower limit of this tumor mass two small openings were found which readily admitted a fine probe and from which exuded a watery secretion. Below this circular area, in the region of the external genitalia, were two folds of mucous membrane situated opposite each other on either side of the midline. Immediately above these folds and slightly medial to them but below the circular tumor were two openings 2 mm. in diameter, one on either side of the midline. A plug of grayish, tenacious mucous protruded from each opening. These admitted a probe for about 5 cm. The anal opening was patent. The sex of the child could not be determined.

Posteriorly, in the lumbar region, extending down to the sacrum, there was a noticeable widening of the vertebral column, with a central depression and apparent absence of spinous processes.

The infant progressed normally on breast and bottle feedings until the fifth day, when it was noticed that the abdomen was distended. Roentgenograms were taken at this time by Dr. Ackermann. The distention persisted despite treatment. No masses were felt, and the bowels moved several times daily. The bowels were filled with gas and presented the appearance of paralytic ileus. The abdominal distention progressed, the skin of the abdomen became very tense and shiny, and

the infant was unable to retain food. There was definite circulatory and respiratory embarrassment, due to the distention, and the infant grew weaker and died on the twelfth day.

An abbreviated report of Dr. Palmer's postmortem observations follows:

There were no abnormalities in the heart or in the lungs.

A large hollow viscus filled the entire general abdominal cavity. The liver was found in the left hypochondrium, but the relation of the right and left lobes was not reversed. The gallbladder and ducts were in normal relation to the liver and duodenum. The cecum was immediately beneath the liver to the left of the midline. The stomach was of normal size and shape and was found in the normal position. The spleen was in the normal position and behind the liver. The large viscus was the entire large intestine, except for a small part of the cecum and rectum. It was an enormous megacolon. On removing the viscus, a defect was found in the structure of the vertebrae in the midabdominal region. There was practically maldevelopment of the bodies of the lumbar vertebrae. The colon was intimately attached to these abnormal structures and was separated with difficulty. The sympathetic chain could not be demonstrated. The abnormal condition in the lower portion of the abdomen was a complete exstrophy of the bladder, which was described in the history. The two openings in the bladder were ureteral openings. The right ureter was dilated in the lower portion and the left bifurcated in the upper portion 1.5 cm. below the pelvis. The right kidney had a complete posteriorly placed pelvis, so that the hilus was on the posterior flat surface. The two openings below the exstrophied bladder led into two separate, but attached, muscular cylindric structures which were 5 cm. in length. That these structures made up a double uterus is proved by the fact that a typical tube continued from the distal extremity of each and a round ligament passed through the inguinal canal to the position of the labia majora. An ovary was found on each side adjacent to the tube.

The pathologic diagnosis was: exstrophy of the bladder; bifurcation of the ureter (left); dilatation of the ureter (right); misplacement of the liver without transposition of the lobes; megacolon; congenital malformation of the lumbar vertebrae and interference with the nerve innervation of the colon; double uterus, and double vagina.

A Case of Myelitis and Encephalitis Following Measles. Dr. Edwin P. Russell and Dr. Bert I. Beverly.

A girl, aged 6 years, was first seen on July 10, 1931, because of severe headache and muscular twitchings which had developed during the preceding night. She was convalescing from measles and had been free from fever for about four days. She had not had a severe attack of measles; no physician had been summoned, and no medication was given.

On examination the temperature was 102.4 F., orally. The respirations were irregular and rapid, from 40 to 50 per minute, and there were involuntary arhythmic contractions of both upper extremities and shoulders with marked coarse tremor of the hands. There was slight rigidity of the neck. There was no nystagmus, strabismus or extra-ocular palsy, and the pupils reacted to light. The eyegrounds were normal. The throat was slightly reddened, and the ear-drums were dull but not bulging. The heart, lungs and abdomen exhibited no abnormality.

All of the tendon reflexes were present, and the left knee jerk was overactive. There was no Babinski sign or ankle clonus. Lumbar puncture was done. The spinal fluid, which was under increased pressure, showed 300 cells per cubic millimeter and 2 plus globulin.

The muscular contractions were less severe on the following day, the knee jerks were absent, and there was difficulty in urination. On July 13 paresthesia of both hands had developed, and the patient had urinary and fecal incontinence and paralysis of both legs. The intercostal muscles were also paralyzed, and the breath-

ing was purely diaphragmatic. There was loss of all sensation in the skin below the level of the second rib. The child was alert mentally.

On July 14 the patient was seen by one of us (Dr. Beverly), who made a diagnosis of transverse ascending myelitis and encephalitis following measles, with involvement of the respiratory center. At his suggestion a 50 per cent solution of magnesium sulphate was given intravenously daily for three days. The child's condition was poor; she became irrational at times and at other times lethargic and somnolent. The respirations were irregular, and sometimes it seemed that they would cease. The temperature varied from 99.6 to 102 F., but at no time went above this point. She became unable to void and required catheterization three times daily for fourteen days.

The condition remained extremely critical for six days, after which time the respirations became more regular and the patient began to regain the use of the intercostal muscles. Whether this improvement was influenced in any way by the injection of magnesium sulphate it is impossible to say, but it is our impression that it was not. The arms did not become completely paralyzed, but there were marked weakness in the right arm and coarse intention tremor in both for about two weeks.

On July 22 the child began rather abruptly to move her legs. This was followed in five days by a return of rectal control, and four days later she was able to urinate voluntarily. Cutaneous sensation returned more slowly. Mentally she was irritable and would scream and swear on the slightest provocation. She was also very negativistic, and when urged to do something would have a temper tantrum. This was quite unlike her normal personality. At the same time she could hear, understand and speak without difficulty.

As she improved and began to take an interest in her surroundings it was noticed that she could not see well. The retinas were red and the disks a little hazy in outline, but the chief difficulty was paralysis of accommodation. She would pick out letters in the large print of newspaper headlines, but could read nothing in smaller type than this. The pupils reacted to light sluggishly at first and better as time went on, but she did not have a return of acute vision until the early part of October, 1931, three months after the onset of the illness. On August 3 she stood alone, and within a week was walking about the house. The gait was mainly one of weakness and much like that of postdiphtheric palsy. The umbilical reflex was lost early and had not returned six months after the onset. She made a complete recovery in every sense, as the change in personality was temporary, and so far as any one can see she is the same mentally and physically as she was before her illness.

There are two interesting features in this case. First, it is unusual to see both myelitis and encephalitis at the same time following measles. Second, it is unusual to see a patient with such an extensive involvement of the nervous system recover.

From a review of the literature on myelitis, the disease has apparently become more frequent during the past few years, and more cases of recovery are being reported. This increase of myelitis parallels the increase of encephalitis in children.

ATYPICAL BRAIN TUMOR WITH MEGALOCEPHALIA. DR. C. A. ALDRICH.

R. N., aged 6, was a robust boy who had been under my care since birth. In September, 1931, his mother noted that his right eye turned out. She consulted an ophthalmologist, who prescribed glasses and advised exercise of the right eye by covering the other part of the time. It was noted also that he became less active and liked to play with girls more than with boys.

The previous history was not pertinent. He weighed 55 pounds (24.9 Kg.) and was 49 inches (124.5 cm.) tall.

In October, 1931, he came to me because he had vomited several times in the early morning, was awkward on his feet and drooled, and because his speech was impaired.

On physical examination it was found that he had marked ataxia of the legs, slight ataxia of the arms, exaggerated knee jerks, a positive Babinski reflex on both sides, a tendency to clonus in both ankles, right lateral strabismus, nystagmus in both eyes, deviation of the tongue to the left and typical scanning speech. In all other respects physical examination gave negative results. Because of these findings and the history of morning vomiting, I suspected tumor of the brain and asked for consultation. Dr. L. J. Pollock observed the child in Passavant Hospital for a week. The spinal fluid was not under increased pressure and showed no serologic or other abnormality. Roentgenograms of the skull showed no evidence of increased intracranial pressure. The eyegrounds were normal. During this time the ataxia of the arms improved to such an extent that the patient's mother and school teacher could detect no deviation from his usual signature and he was able to do detailed work with his fingers such as cutting out pictures and solving puzzles of various sorts. The ataxia of the legs was thought to be improved, and the drooling stopped. The leukocytes numbered 10,000, and the temperature at no time exceeded 100 F. rectally. Because of this definite improvement and in spite of the negative results of examination of the spinal fluid, it was thought that the most probable diagnosis was subacute or chronic encephalitis of low grade.

The patient was put to bed at home with a trained nurse, and on the next day he complained of headache for the only time in his entire illness. This was thought to be the result of the spinal puncture. The symptoms during the next four months were more pronounced in the lower extremities, which became more spastic. The unusual feature was that results of examinations varied extremely from week to week. On one observation the left leg would be normal, and on another the right, and again both would be spastic and marked clonus would be elicitable. After six weeks the child could not walk, even with support. During this period he vomited occasionally at various times of the day, lateral strabismus of the left eye developed, he began to have trouble in chewing and swallowing food, and the scanning speech became more and more inarticulate. He was at no time dull or drowsy, and none of his attendants noticed any psychic changes. He played actively with his hands. Treatment consisted in the administration of arsenic, atropine, nonspecific protein and magnesium sulphate at different times.

Early in March, about five months after the onset, facial paralysis was first noticed on the left side. This moved to the right side and then disappeared, but returned in the terminal phase. Contracture in the legs made it advisable to apply casts, and the difficulty in swallowing made us resort to feedings by tube. On March 18, the child suddenly had an attack in which he became cyanotic, had sharp contraction of the entire left side of the body and went into coma, and Cheyne-Stokes respiration gradually developed. He was taken to the Evanston Hospital, where 30 cc. of 50 per cent dextrose solution was given intravenously, apparently with no beneficial effect. Dr. Pollock and I saw him late in the evening and gave an immediately bad prognosis to the parents. However, in the morning he was out of coma and as bright as ever, but still breathed irregularly. The spastic involvement of the left leg continued, but the arm, as well as the left side of the face, became limp and paralyzed. It became possible to dispense with feeding by tube, and the patient again went home. Head drop became apparent at this time.

On March 31, he again had an attack in which he became unconscious for a few moments, but for the most part he improved until April 9, on which day a vomiting attack ushered in coma, Cheyne-Stokes respiration and a gradual failure of respiratory effort. He died on that night.

This report is given because of the unusual clinical picture and diagnostic difficulties both before and after death. The diagnosis rested between encephalitis, tumor of the brain and multiple sclerosis. The last condition was ruled out because it does not occur in young children. Against encephalitis were the negative results of examination of the spinal fluid and the afebrile course. Against brain tumor were the normal eyegrounds, the absence of headache and the fleeting character of the symptoms.

Autopsy was performed by Dr. Gunn, and the brain is being studied by Dr. Arthur Weil in the Neurological Pathology Laboratories at Northwestern Medical School. A preliminary report from this laboratory was: infiltrating glioma of the midbrain and cerebellum, with megalocephalia.

EPIDEMIC VOMITING. DR. J. L. REICHERT.

A girl, aged 4½ years, had a pernicious type of vomiting during an infection of the upper respiratory tract. The vomiting was associated with watery diarrhea, acetonuria, an odor of acetone in the breath and hyperpnea. Except for a red throat there were no other abnormal physical findings. No alkalis were given. In spite of the typical clinical picture of acidosis, chemical examination of the blood revealed the signs of marked alkalosis.

The case is presented in order to show that epidemic vomiting is not always acidotic, to point out the similarity, symptomatically, of acidoses and alkaloses, and to raise the question of the advisability of giving alkalis in so-called epidemic vomiting.

TUBEROUS SCLEROSIS. DR. JOHN S. MCDAVID.

The first cases of tuberous sclerosis were reported by Bourneville in 1880, who described ten cases. Since that time there have been reports by various authors in different countries. The condition is also known as Bourneville's disease, and in all there have been described about eighty cases. I believe that the most recent report on this subject was given by Yakovlev and Gutherie (*Arch. Neurol. & Psychiat.* **26**:1145 [Dec.] 1931). Tuberous sclerosis is a congenital anomaly of the brain and other organs, characterized clinically by idiocy and epilepsy and pathologically by multiple sclerotic nodes over the surface of the brain, multiple subependymal tumors and multiple tumors of the heart, kidneys, skin and other organs.

In January, 1931, I was called to see a boy, aged 6, who was obviously an idiot and whose mother gave me briefly the following history:

The child was born of a healthy mother and father. The family history was unimportant. The delivery was instrumental, though not difficult, and took place in a hospital. The weight at birth was 6 pounds and 5 ounces (2,869.3 Gm.), and the child appeared to be normal. Although breast fed, he developed poorly, and at 6 weeks of age weighed only 4 ounces (113.4 Gm.) more than at birth.

When 6 months old the child had a severe tonic convulsion. He had not been ill and had no fever. The convulsion lasted for three minutes, and during this time he was rigid and blue and seemed to have difficulty in breathing. Three weeks later he had a similar attack. Following this the seizures were progressively more frequent and severe. At 18 months he was having from six to ten generalized convulsions daily. From this age on the attacks became less frequent and disappeared entirely after he was 3 years old. The description of the later convulsions was that of atypical epileptiform seizures. They seemed to be helped somewhat by the administration of phenobarbital. During the patient's infancy the mother had given him large doses of phosphorized cod liver oil and a moderate amount of orange juice.

At the age of 1 year a rash began to develop about the nasolabial fold on the right cheek. A physician told the mother that this rash was made up of multiple sebaceous adenomas.

The child sat up at 20 months and walked for the first time at 3 years. He was always incontinent as to both urination and defecation and never learned to talk or to feed himself. During the last two years of his life he learned to point toward desired objects. A week previous to my first visit he was taken acutely ill with a high temperature, vomiting and diarrhea.

Physical examination showed an extremely emaciated, dehydrated child with an enormously distended abdomen. No rash was evident on the face at this time

The throat had a scalded appearance, and there was a distant acetone odor to the breath. The abdomen was of boardlike rigidity, silent to auscultation and tympanitic on the right side but somewhat dull on the left. All the normal muscular reflexes were present; no pathologic muscular reflexes were found. There was marked incoordination of voluntary movements, and there seemed to be an intention tremor of the arms and hands. The child was removed to the hospital, and after an enema and turpentine stupes, a mass could be palpated in the region of the left kidney. The parents refused operation and the patient died two days following his admission to the hospital.

Autopsy was performed by Dr. Piette, the pathologist, six hours after death. Mention will be made only of the findings outside of the brain. There were generalized peritonitis caused by cystic degeneration and rupture of a large rhabdomyoma of the left kidney. The right kidney contained many small cystic and nodular tumors of the parenchyma, and there was a small cystic tumor of the heart muscle. Streptococcus hemolyticus was obtained in culture of the pus in the abdominal cavity. The brain was studied by Dr. G. B. Hassin, who has given the following report:

"The frontal poles of the brain were somewhat smaller and whiter than usual. Over the surface of the temporal, parietal and occipital lobes were numerous, irregular, white areas that projected above the general contour of the convolutions. They were flattened, much more firm than the surrounding brain tissue and some of them appeared umbilicated. These areas were fairly well circumscribed, about a centimeter in width and bounded by the tertiary fissures. Microscopically, they were found to be made up of very large atypical glial cells with innumerable glial fibers intertwined in every direction. Typical ganglion cells were also present in these areas, being scattered irregularly here and there. The hippocampus, cerebellum and brain stem were normal."

Osteomalacia or Late Rickets. Dr. Gerard N. Krost.

A boy, aged 10, with severe deformities of osteomalacia, curvature of the extremities, scoliosis and similar symptoms, was treated as an outpatient at the dispensary of Northwestern University Medical School. In the previous history these points are outstanding: He was exclusively breast fed for eleven months and had received no milk and little vegetable since weaning, until the age of 10 years. No cod liver oil was given during infancy. He had diarrhea at 2 years of age which persisted for more than a year. The diagnosis at that time was tuberculous peritonitis. The deformities were first noticed at the age of 7 years. He then received treatment with a quartz lamp for two years. At the dispensary he was given 9 drops of viosterol daily. This small dose is explained by the fact that at that time great fear was felt as to its toxicity. Doses of 15 drops were given later for eight months, of 30 drops for two months and of 40 drops for fifteen months. When investigation proved viosterol safer than had been supposed, 40 drops of a "1000X" preparation were given daily. This preparation had two and a half times the D potency, or really 2,500 D. Doses of 80 drops were given for eight months. This amount was comparable in terms of viosterol in oil 250 D to 26 cc., or 780 drops.

Roentgen examinations were made at frequent intervals, and little if any improvement was seen from the time of the patient's entrance to the hospital to the last observation. The patient died of nephrosis, and necropsy was not permitted.

In the pathogenesis of this patient's condition the long continued diarrhea with loss of fat, which influenced the calcium metabolism, had a bearing as well as the unbalanced diet and lack of vitamin D. Much larger doses of viosterol than are available in ordinary commercial preparations are needed in severe rickets and osteomalacia. Much larger doses should probably have been given to this patient, but without determinations of blood calcium there was no guide as to the amount necessary or safe. Treatments with a quartz lamp were given from

the eighth to the tenth year of age, every other day for nearly two years, with a steadily downward course. The patient was unable to walk without crutches.

The conclusions to be drawn from this case are: In osteomalacia or late rickets treatment with the quartz lamp does not effect a cure. Large doses of viosterol must be used to cure severe rickets or osteomalacia. Larger doses than were used in this case may be necessary. The dosage should be controlled by determinations of blood calcium in order to determine the correct amount of viosterol, and as a factor of safety as well.

NORTH PACIFIC PEDIATRIC SOCIETY

L. HOWARD SMITH, M.D., *Secretary*

Twenty-Seventh Semi-Annual Session, June 25, 1932

A. HOWARD SPOHN, M.D., *President, in the Chair*

ROENTGEN DEMONSTRATION OF VARIOUS CONDITIONS. DR. ALAN HUNT, Tacoma, Wash. (by invitation).

A series of roentgenograms of children demonstrating tuberculous and non-tuberculous conditions of the lung, tumors of the brain, hydrocephalus and comparative conditions of the bones in rickets, scurvy and syphilis was presented.

FAMILIAL MALDEVELOPMENT OF TEETH. DR. R. S. MILES, Tacoma, Wash.

A boy, aged 6 years, presented a condition of congenital absence of enamel. The mother had poor teeth, as had also the maternal grandmother. The father and all members of the father's family had good teeth. The patient had three older brothers (11½ years, 10 years and 8 years old) and a sister 15 months of age. Every other child in the family had poor teeth; development had otherwise been normal. The teeth had erupted normally but had showed absence of enamel. They showed wearing and flattening. The roots appeared normal in the roentgenogram. The blood calcium was 15 mg.

DISCUSSION

DR. J. I. DURAND, Seattle: Have you found any cases in the literature? Is there deformity of any other bones?

DR. R. S. MILES, Tacoma, Wash.: A roentgenogram of the jawbone shows it to be normal.

DR. A. S. MCCOWN, Seattle: Is there any history of rickets?

DR. R. S. MILES, Tacoma, Wash.: The patient and his sister, aged 15 months, who shows the same maldevelopment, have had a proper diet since birth. The mother received the proper diet during pregnancy. I do not know what causes the congenital absence of enamel. The teeth erupt like pegs and then are gradually flattened out.

DR. A. REMBE, Seattle: This case brings up the subject of early caries in young children. I am reminded of a girl aged 2 years whose molars had no enamel. From the age of 1 year she had received no milk. Lately not enough milk has been used. Every adult should drink one pint of milk daily. Surely every infant should have it. The drinking of more milk will help to prevent dental caries.

DR. J. I. DURAND, Seattle: Eighteen years ago acid secretion in the mouth was thought to be the chief cause of dental caries; now it is believed that vitamins are extremely important for prevention. In the last eighteen years the Seattle school children have shown a 20 per cent improvement in the number of cases

of caries. Rickets has some influence on the development of the teeth. Some malformation is usually seen in any severe case of scurvy or rickets. Three years ago Mellanby believed that overfeeding of carbohydrate was one of the greatest factors in the development of dental caries. In civilized countries the teeth have a tendancy to decay. The natives of New Zealand had only 2 per cent dental caries. The same people under civilized conditions have poor teeth. We should be able to find the cause of dental caries and prevent it.

DR. E. A. LAYTON, Tacoma, Wash.: Are the second set of teeth just like the first?

DR. R. S. MILES, Tacoma, Wash.: Yes. They may have a slight film of enamel, but this soon wears off.

DR. N. W. CLEIN, Seattle: Just what is the importance of milk in the prevention of dental caries? The Eskimos and the coolies in China drink no milk and yet have good teeth. There is a colony in Germany where no meat is eaten, nor milk is drunk. Four hundred children in this colony have been studied, and they all show fine teeth and no rickets.

TREATMENT OF NEVI WITH DRY ICE. DR. H. T. CLAY, Tacoma, Wash.

Dry ice, used commercially by ice-cream companies and dairies, may be used as a substitute for carbon dioxide snow. It is cheap, easy to handle and can be shaped with a knife. As yet only the bulbous type of nevi has been treated with this substance, with satisfactory results. (Five cases were demonstrated, to show results and the method of treatment.)

PYKNOLEPSY AND PETIT MAL. DR. D. M. DAYTON, Tacoma, Wash.

Two patients were presented, both of whom had several attacks a day of brief loss of consciousness or partial loss in which they did not fall or entirely lose automatic movement. They were both in good general health and were normal mentally.

CASE 1.—A girl, aged 10 years, had been having several mild spells a day for four years prior to presentation. The spells lasted for five or ten seconds, during which she never fell, dropped things, rolled her eyes or had twitching of the muscles. She was bright, active and cheerful, and there had been no apparent deterioration during the four years of the attacks. The attacks were unaffected by phenobarbital.

CASE 2.—A boy, aged 4½ years, had been having from four to six attacks a day for six months. His spells were brief and mild. He never fell, but was at least partially unconscious for a moment; at times there was some jerking of an arm. The attacks were controlled by phenobarbital.

The second case was ordinary petit mal, whereas the first case fits into the description of pyknolepsy as given by Adie: "A disease with an explosive onset between the ages of 4 and 12 years, of frequent short, very slight monotonous epileptiform seizures of uniform severity which recur almost daily for weeks, months or years, are uninfluenced by anti-epileptic remedies, do not impede normal mental and physical development, and ultimately cease, never to return."

DISCUSSION

DR. A. S. MCCOWN, Seattle: Is there any family history of epilepsy?

DR. D. M. DAYTON, Tacoma, Wash.: There is no history of epilepsy or of similar attacks in either family.

DR. L. LEWIS, San Francisco: Is there ever any coldness or blueness of the extremities?

DR. D. M. DAYTON, Tacoma, Wash.: No.

DR. J. H. SKINNER, Yakima, Wash.: I wish to report a case of epilepsy in a child who for three years had from five to fifteen attacks daily. She was then given daily chiropractic treatment and for food only orange juice for a few weeks. During the last three or four months she has been entirely free from attacks.

DR. A. H. SPOHN, Vancouver, B. C.: I should like to report a case of pyknolepsy which increased when the patient was 19 years old. Now, after several years have passed, the patient is entirely well. She has a niece who has marked epilepsy. This is another case in a girl who has had from seven to eight attacks daily for the last six years. She is an expert swimmer, and there is no deterioration mentally.

DR. L. LEWIS, San Francisco: The most important thing in epilepsy is the question of mental deterioration. It may not come for several years, or it may come suddenly, with no relationship to the number or the severity of the attacks. Phenobarbital is not satisfactory in the treatment of petit mal.

DR. A. REMBE, Seattle: Inducing mild acidosis has been most satisfactory in the treatment of epilepsy.

DR. J. I. DURAND, Seattle: Dr. Abt's suggested treatment of tricalcium phosphate and calcium lactate given daily over long periods seems to give marked improvement.

DR. E. A. LAYTON, Tacoma, Wash.: I am much interested in the question of school attendance with these epileptic patients. Many of them, after they have been kept out of school for from three to six months under treatment, are allowed to return with the instruction that they will have to stop school if they have any more attacks. It is surprising to see what self-control can do in preventing attacks.

DIABETES COMPLICATED BY ACUTE INFECTION. DR. F. A. H. JOHNSON, Tacoma, Wash. (by invitation).

A girl, aged 4 years, with severe diabetes had been treated for two years with insulin and restriction of diet, with satisfactory results. Suddenly a high temperature and leukocytosis, 26,000 leukocytes, developed. The cause of the acute infection could not be determined, and the patient died within thirty-six hours.

Dr. Dale Martin of Tacoma, Wash., made the postmortem examination and reported that the only pathologic observation was an extreme grade of lymphoid hyperplasia of the intestinal tract.

PROBLEMS OF WATER METABOLISM (LANTERN SLIDES). DR. TEMPLE FAY, Philadelphia (by invitation).

Comparative anatomy shows that the cerebrum of man is more developed than that of other animals. But in the child at birth the cerebrum is not fully developed, and only massive lesions in the hemispheres give symptoms. Cerebrospinal fluid dialyzes from the choroid plexus and is absorbed through the subarachnoid space. Blocks produce internal hydrocephalus, with ironing out of the sulci of the cortex. The chief law in hydraulics of the brain is that there is equal distribution of pressure in the system. Pressure of fluid is equalized over the brain. Vomiting is mainly a reflex action of the brain. The pacchionian bodies absorb the cerebrospinal fluid. Absorption may be obstructed by red blood cells or leukocytes. Deficiencies of venous drainage are seen in cases of mental deficiency. Blocking of the venous canals causes edema of the brain. When the filter bed is blocked, the sylvian area is compressed, causing pressure atrophy. The lower frontal, temporal and occipital areas of the cortex escape. In thrombosis, the area supplied by the blood vessel shows atrophy. This is different when the cause is hydraulic changes. The cranium is a closed container which holds brain substance, cerebrospinal fluid and blood. When one of these is increased it is at the expense of the other two. Thus, when the cerebrospinal fluid is suddenly increased, blood circulation

of the brain is decreased. The same is true in edema of the brain. Dehydration improves the circulation of the blood and of oxygen, with resulting improved function of the brain. The wet brain must be dehydrated. The intake of fluid in the affected child must be markedly curtailed. I have fed such a child, 5 weeks old, only 12 ounces (355 cc.) of total fluid in twenty-four hours, with good results. Fluid is eliminated from the body by way of the lungs, the bowels, the skin and the kidneys. In thymolymphaticus the enlarged thymus may compress the jugular veins, causing venous dilatation in the brain, with convulsions, coma and death. In thymolymphaticus it is a question of adequate cerebral drainage and venous blocking. The cerebral mechanism is influenced by (1) the amount of oxygen delivered, (2) venous drainage and (3) the fluid factors which come and go. Vomiting and stupor are due to what Roundtree has called "water intoxication." The best ways to dehydrate are by (1) purgation, (2) blood-letting and (3) sweating.

DISCUSSION

DR. A. H. SPOHN, Vancouver, B. C.: Concerning status lymphaticus, infants die suddenly but quietly in the first year of life, with no evidence of struggle. How does Dr. Fay explain these deaths?

DR. R. S. MILES, Tacoma, Wash.: A child with stupor, delirium or coma shows marked dehydration; yet one tries to dehydrate another child showing the same symptoms. How are these similar symptoms explained?

DR. A. S. MCCOWN, Seattle: I should like to ask Dr. Fay why it is that in cases of encephalitis with convulsions in which there is no increased pressure of the cerebrospinal fluid there is relief of symptoms when the fluid is withdrawn.

DR. N. W. CLEIN, Seattle: I have been treating four cases of Little's disease by repeated cisternal and lumbar punctures every two or three weeks, withdrawing 25, 50, 75 or 100 cc. of fluid at a time. Two of the four babies appear normal one and 2 years later, while the other two are not so fortunate.

DR. A. H. SPOHN, Vancouver, B. C.: Are cases of petit mal due to changes at the time of birth? Will Dr. Fay be good enough to tell us something about water balance in the treatment of epilepsy?

DR. TEMPLE FAY, Philadelphia: In cases of thymic death, especially when ether is given, there are edema of the brain and convulsions. Death is due to the fact that blood fails to reach the brain, or that there is failure of function due to failure of oxygen to reach the centers. As to dehydration and cerebral symptoms, peripherally the infant may look dehydrated as in severe diarrhea. One can have a wet brain and a dry skin. Dextrose metabolism must be taken into consideration. Glycogen is stored in the brain as in the liver, so that fluid is held in the brain when other tissues are dehydrated. In cases of encephalitis without increase of spinal fluid pressure, the drawing off of the cerebrospinal fluid allows blood to enter the brain, thus there is clinical improvement. In cases of spastic paraplegias, from 30 per cent to 40 per cent mental improvement had been obtained by repeated spinal tappings. By this procedure the brain substance that remains is protected and improved. Petit mal persists in spite of drugs, dehydration, ketogenic diet and other therapy. Epilepsy has to do with circulation. In treatment (1) phenobarbital, (2) dehydration and (3) ketogenic diet should be utilized. Mental deterioration, which is the end-point of epilepsy, not the convulsion, is the most important consideration of the disease. Our results so far have been: 11 per cent cured, 65 per cent improved and 23 per cent failures.

SOFT CURD MILK. (DEMONSTRATION). MR. CARL WALLACE, Tacoma, Wash. (by invitation).

Curd tension as determined by Hill's method is influenced by various processes. Drying, condensing or sterilizing cow's milk has a profound effect on the character of the curd. Readings made on lactic acid milk, S.M.A., protein milk, Similac, Dryco, lactogen, Klin, nonallergic milk, Eiweiss milk, Eagle brand and

several makes of evaporated milk all gave uniformly soft curds. If the curd tension of the original milk is not too high, the modification of boiling, diluting and adding of carbohydrates will give a final product with a comparatively low curd tension. Homogenization decreases the curd tension approximately 50 per cent. If a milk of low specific gravity and low curd tension is homogenized, with the resultant subdivision of the fat globules and the reduction of the curd tension to 10 Gm. or lower, a raw milk very suitable for infant feeding should result.

DISCUSSION

DR. H. T. CLAY, Tacoma, Wash.: Homogenized milk has given good clinical results in cases of difficult feeding. It is possible to explain the sudden vomiting of certain infants by the fact that they have accidentally been given some hard curd milk. Homogenization makes it possible to use a soft curd milk without having to boil the milk.

DR. W. F. PATRICK, Portland, Ore.: I do not see the necessity for homogenized milk. Evaporated milk is entirely satisfactory.

DR. V. W. SPICKARD, Seattle: I should think the chief objection to homogenized milk would be the expense. Boiled or evaporated milk is satisfactory. I cannot see the advantage of the added expense of raw, soft curd milk.

DR. C. LUVERNE SMITH, Seattle: Mr. Wallace brought out the fact that the addition of carbohydrate gave a low tension curd. I should like to ask which type of dextrimaltose was used.

DR. M. L. BRIDGEMAN, Portland, Ore.: Is the curd tension lowered with lactic acid milk or Bulgarian milk?

DR. R. S. MILES, Tacoma, Wash.: What is the difference in cured tension of goat's milk and cow's milk? Does the milk from a herd of cows have the same curd tension or does it vary with the type of feeding?

DR. A. H. GRAY, Seattle: What is the difference in curd tension in pasteurized and boiled milk?

DR. N. W. CLEIN, Seattle: What about the bacterial count of homogenized milk? Homogenization does not tackle that problem. Cow's milk was meant for the calf. There are many things to be considered about cow's milk before it is fit food for the baby. What is the curd tension of so-called "pooled milk"?

DR. A. H. SPOHN, Vancouver, B. C.: Cows fed irradiated yeast give milk with a soft curd. It would not be necessary to homogenize such milk. Most problems of feeding are now more difficult than ever, so the soft curd milk may have some decided advantages.

MR. CARL WALLACE, Tacoma, Wash.: Boiling the milk is satisfactory, if the curd tension is not too high to start with. Lactic acid milk and Bulgarian milk both give a low curd tension. Goat's milk curd is the same as cow's milk curd as to tension. Tension of the curd is modified by the content of moisture in the cow's food. The bacterial question must be taken care of by pasteurization. Pooled milk will vary from 50 to 130 Gm. in tension. Why homogenize a soft curd milk? Breast milk is considered zero; it is reasonable to suppose that the nearer one approaches breast milk, the better.

NORMAL DEVELOPMENT IN DIABETIC CHILDREN: DIABETIC COMA. DR. LESTER PALMER, Seattle (by invitation).

One hundred per cent of the diabetic patients can be made 100 per cent efficient. We should make every effort to offset the impression that the diabetic patient cannot be cured. It is most important to make an early diagnosis and institute proper treatment. Diabetic coma is an emergency, and the family of the diabetic patient must be able to recognize the condition early. When the diabetic child vomits, the doctor must be called immediately. There is no need for the diabetic patient to die in coma. When he has an infection, he can be handled as the

nondiabetic patient, if treated early. The diabetic child withstands surgical measures better than the nondiabetic child. When the diabetic child is in coma, he should be given from 40 to 100 units of insulin immediately, while arrangements are being made to send him to the hospital. There are two things to treat the patient for: acidosis and dehydration. Give 1,500 cc. of fluid within the first hour. Empty the stomach and bowel and support the circulation. The emphasis should be placed on: (1) early treatment, (2) correct treatment and (3) close observation. It is not right to say that diabetes cannot be cured.

ATRESIA OF THE ESOPHAGUS. DR. J. S. BACKSTRAND, Salem, Ore.

A baby girl, delivered by cesarean section and resuscitated with difficulty, on the fourth day of life vomited after nursing. Vomitus was ejected from the nose and mouth, breathing stopped, and the patient became markedly cyanosed. As soon as the nasopharynx was cleared of milk by holding the patient's head downward, she appeared normal, except that at each nursing the vomiting recurred. After a few stools of meconium, there was no further bowel movement except for a small amount of mucus.

A small catheter passed into the esophagus met an obstruction 8 cm. from the margin of the lip. Fluoroscopy showed the barium ending in a blind pouch at the level of the clavicle. A gastrostomy was done as a final gesture. As soon as food was placed in the stomach, the infant had the same kind of an attack as when the milk was given by mouth.

A roentgenogram taken after a thin barium mixture was inserted into the stomach showed the esophagus filled to the level of the third rib anteriorly and revealed the presence of an extensive pneumonia. The patient died on the ninth day of life, the day following the operation.

Autopsy showed the upper portion of the esophagus ending in a blind pouch at the level of the clavicle. The lower portion of the esophagus was normal in appearance and extended upward to enter the trachea through an orifice 0.5 cm. in diameter at a distance of 1 cm. below the bifurcation. The lungs showed aspiration bronchopneumonia.

The symptoms are fairly constant in all cases of atresia of the esophagus and follow closely Brenneman's clinical description of the anomaly: (1) aspiration asphyxia at birth, with considerable mucus in the nasopharynx, (2) immediate regurgitation and cyanosis at each attempt to nurse, (3) rapid loss of weight, (4) absence of stools or very small stools after meconium had been passed, (5) distention of the abdomen from air passing through the tracheo-esophageal fistula and (6) complete obstruction of the esophagus as shown by roentgenograms, and the failure to pass a sound or catheter beyond the obstruction.

Roentgenograms and a specimen are shown.

BOOK REVIEWS

Die Behandlung der Kindkrankheiten mit Ultraviolett- und Röntgenstrahlen. By Prof. Dr. W. Birk and Dr. L. Schall. Price, 12 marks. Pp. 256, with 45 illustrations. Berlin: Urban & Schwarzenberg, 1932.

This book takes up in a comprehensive way the various diseases of children in which the ultraviolet rays or the x-rays are advocated as a treatment.

The book is divided into two parts, the first dealing with the ultraviolet rays and the second with the x-rays. Under each part the various methods of production and the properties of the ultraviolet rays and the x-rays are outlined, and the method of measurement of dosage is given. Also, the harmful effects that may complicate this form of therapy are dealt with in full.

Under each division the various diseases discussed are described and classified, and the methods of treatment are outlined. If indicated, the exact procedure, dosage and dangers of the ultraviolet rays and the x-rays are stated. Numerous cases illustrate the foregoing points.

As befitting their great importance, the subjects of rickets, tuberculosis and leukemia are dealt with in great detail. Other diseases dealt with under ultraviolet treatment are spasmophilia, infected wounds, whooping cough and asthma. Those discussed under roentgen treatment include Hodgkin's disease; malignant tumors; diseases with an increased bleeding time, such as hemophilia; diseases of the central nervous system, such as tumors of the brain, hydrocephalus, feeblemindedness, postencephalitis and epilepsy; diseases of the glands of internal secretion, as of the thymus, pituitary gland, thyroid, parathyroid glands and suprarenals; pyloric spasm; lymphatic tissue of the throat, including the tonsils; bronchial asthma; bronchopneumonia; acute inflammation, such as boils, phlegmons, infected glands and abscesses of the breast, and hemangiomas.

The book is concise but complete in every detail and is an excellent reference in regard to ultraviolet and roentgen therapy.

Childhood Type of Tuberculosis. Report of Ten Years' Activity at Lymanhurst School for Tuberculous Children. Price, $1. Pp. 141, with illustrations. Minneapolis: 1932.

In 1921, the Lymanhurst School for Tuberculous Children was established in Minneapolis: (1) to provide educational facilities for tuberculous children who were able to attend school and (2) to carry out a careful and prolonged study of tuberculosis. The present volume is a condensed report of the activities from 1921 to 1931, and gives a brief résumé of the research completed during that period. This comprised studies on such subjects as mental and nervous states, the heart, the gastro-intestinal tract, the bones and joints, exposure and infection, the lymph nodes, pleurisy, pulmonary lesions and relapses. More extensive reports are given illustrative of the childhood type of pulmonary tuberculosis. These are well illustrated by roentgenograms. An extensive bibliography is appended. While the volume is far from being a complete presentation of tuberculosis as it occurs in children, it furnishes information of interest to special students of the subject and corrects some false impressions which, in spite of the recent literature and teaching, are still extant among practitioners.

Vitamins: A Survey of Present Knowledge. Privy Council Medical Research Council, Special Report Series No. 167. Price, 6 shillings, 6 pence. Pp. 277, with 34 illustrations. London: His Majesty's Stationery Office, 1932.

This publication presents the present knowledge of vitamins in a complete and detailed manner. Contributions concerning vitamins in the literature of all

countries have been carefully reviewed, and the entire material has been collected and presented in concise form. The numerous experimental studies which have gradually developed the modern conception of vitamins are carefully recorded. Each of the known vitamins is discussed in a separate chapter, which includes clinical observations as well as basic scientific data. The relation of vitamins to dental tissues is considered in detail. The chapter on human diets consists of a discussion of many foods and diets in various countries from the standpoint of their vitamin content. The vitamin requirements of mother and infant are especially stressed. There is included a long list of foods with tables showing their relative content of each of the vitamins.

Classic Descriptions of Disease. By Ralph H. Major, M.D. Price, $4.50. Pp. 630. Springfield, Ill.: Charles C. Thomas, 1932.

This most unusual and pleasing volume should be a part of every medical library. In the past few years we have been so used to thinking of the advance of medicine as a series of laboratory experiments that we have almost overlooked the factor most essential to medical advance, accurate clinical observation.

No book with which the reviewer is familiar has traced this clinical observation from its beginnings on as does this book. It is interesting to follow through the various descriptions and different phases of disease pictures by the various writers from centuries ago up to the present time. One is struck by the amount of reading that the author must have done and the intelligent way in which he must have chosen his reading.

The book is well illustrated and should be an inspiration to clinical teachers and clinical observers. In this day of high prices, the price, too, is quite unusual.

The Child from One to Six: His Care and Training. United States Department of Labor, Children's Bureau. Bureau Publication No. 30. Paper. Price, 10 cents. Pp. 150. Washington, D. C.: Government Printing Office, 1931.

This publication is well planned and written for the instruction of parents in the care and training of preschool children. It is easily read and understood and is practical and concise throughout, although covering the subject completely. The material conforms to the latest developments of pediatrics of the present time.

The discussions on mental development, psychologic aspects and habits of eating, sleeping and play are handled in a sound and constructive manner, showing a wholesome understanding of the subject.

Advice on food, clothing and surroundings is practical and to the point. The development and maintenance of good health are emphasized, with due space devoted to the prevention of disease and the care of the sick child.

A list of selected books of interest to parents is included.

Radiological Study of the Para-Nasal Sinuses and Mastoids. By Amedee Granger, K.C.B. Price, $5.50 net. Pp. 186, with 113 illustrations. Philadelphia: Lea & Febiger, 1932.

This book describes two positions, determined by a series of experiments, which show the bony landmarks of all the sinuses. There are sixty-two pages of illustrations, fully described, which exemplify the diagnostic points. The book gives an accurate means of diagnosing the various diseases of the paranasal sinuses.

The various positions for taking films of the mastoid are evaluated, and the technic Granger describes for making petrous views of the mastoid is useful because of its ease for the patient and its diagnostic value. The various points of diagnosis are shown by many illustrations. This is a comprehensive study of the paranasal sinuses and mastoids.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Secretary: Dr. Leonard K. Findlay, 61 Harley St., London, W. 1.
Place: London. Time: July 20-23, 1933.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Henry Gauvain, 125 Harley St., W. 1, London.
Secretary: Dr. E. I. Lloyd, 33 Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Frederic W. Schlutz, Bobs Roberts Hospital, University of Chicago, Chicago.
Secretary: Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Place: Milwaukee. Time: June 12-16, 1933.

American Academy of Pediatrics

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. Thomas B. Cooley, 7815 E. Jefferson Ave., Detroit.
Secretary: Miss Bena M. Henderson, 721 N. 17th St., Milwaukee.

American Pediatric Society

President: Dr. Oscar M. Schloss, 1185 Park Ave., New York.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Washington, D. C. Time: May 8-10, 1933.

Association of American Teachers of the Diseases of Children

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. Oscar Reiss, 1930 Wilshire Blvd., Los Angeles.

Canadian Society for the Study of Diseases of Children

President: Dr. G. A. Campbell, 164 Metcalfe St., Ottawa, Ontario.
Secretary-Treasurer: Dr. L. P. MacHaffie, 162 Clemow Ave., Ottawa, Ontario.

Society of Pediatric Research

President: Dr. Bengt Hamilton, University of Chicago, Chicago.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: New York. Time: May 6, 1933.

SECTIONAL

Central States Pediatric Society

President: Dr. Frank C. Neff, 406 W. 34th St., Kansas City, Mo.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.

North Pacific Pediatric Society

President: Dr. Herbert E. Coe, 509 Olive St., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Horton Casparis, Vanderbilt University Hospital, Nashville, Tenn.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.

STATE

Alabama Pediatric Society

President: Dr. Thomas J. McElhenney, 1722, 2nd Ave., Bessemer.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. M. Hines Roberts, Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, 3503 Prytania St., New Orleans.

Medical Society of State of New York

Chairman: Dr. Brewster Doust, 605 Medical Arts Bldg., Syracuse.
Secretary: Dr. G. C. Sincerbeaux, 6 William St., Auburn.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive, 6 p. m.

North Carolina Pediatric Society

President: Dr. Yates W. Faison, 121 W. 7th St., Charlotte.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 6th St., Tulsa.

South Carolina Pediatric Society

President: Dr. T. D. Dotterer, 1512 Marion, Columbia.
Secretary-Treasurer: Dr. Julian P. Price, 117 W. Cheves St., Florence.

Texas Pediatric Society

President: Dr. Boyd Reading, 2201 Avenue D, Galveston.
Secretary-Treasurer: Dr. F. W. Hoehn, 1006 Medical Arts Bldg., Waco.

Virginia Pediatric Society

President: Dr. St. Geo. Grinnan, 925 W. Grace St., Richmond.
Secretary-Treasurer: Dr. J. B. Stone, 2042 Park Ave., Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. George M. Lyon, 955, 4th Ave., Huntington.
Secretary: Dr. M. F. Petersen, 1013 Quarrier St., Charleston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. E. McClelland, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. P. G. Albrecht, 2009 Adelbert Rd., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.
President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.

Bronx Pediatric Society

President: Dr. Henry M. Eisenoff, 1018 E. 163rd St., New York.
Secretary: Dr. Morris Gleich, 9 Post Ave., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Secretary: Dr. Louis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Archibald L. Hoyne, 25 E. Washington St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. Gordon B. McFarland, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Harold T. Nesbit, Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Bernard Bernbaum, 5057 Woodward Ave. Detroit.
Secretary: Dr. Sarah S. Schooten, 5057 Woodward Ave., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. T. Bolling Gay, 384 Peachtree St., Atlanta.
Secretary: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. William R. Graves, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary: Dr. George F. Kelly, 161 W. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Lewis Webb Hill, 319 Longwood Ave., Boston.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Herbert B. Wilcox, 39 E. 75th St., New York.
Secretary: Dr. John Caffey, 50 Haven Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. Irving McQuarrie, Dept. Pediatrics, University of Minnesota, Minneapolis.
Secretary: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.

Philadelphia Pediatric Society

President: Dr. John P. Scott, 2040 Pine St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. W. E. Chapin, 922 Floyd Ave., Richmond, Va.
Place: Retreat for the Sick, 2621 Grove Ave. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. S. W. Clausen, Strong Memorial Hospital, Rochester, N. Y.
Secretary: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. C. H. Platz, Fort Collins, Colo.
Secretary: Dr. R. H. Verploeg, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. C. L. Smith, 1215, 4th Ave., Seattle.
Secretary: Dr. N. W. Murphy, 515 Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. Donald K. Woods, 2545 4th Ave., San Diego, Calif.
Secretary: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Henry G. Poncher, 5325 Kenmore Ave., Chicago.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: November, 1932.